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ABSTRACT ON INCIDENCE OF ACUTE KIDNEY INJURY AS A COMPLICATION IN CHILDREN WITH SCRUB TYPHUS ADMITTED AT TERTIARY CARE HOSPITAL, VIJAYAWADA

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ABSTRACT

Background: Scrub typhus is an acute febrile illness caused by *Orientia tsutsugamushi* and is increasingly recognized as an important cause of pediatric hospitalization in endemic regions of India. The disease can lead to various complications involving multiple organ systems, including acute kidney injury (AKI), which contributes significantly to morbidity and mortality. Early identification of renal involvement is crucial for improving clinical outcomes. **Objectives:** To determine the incidence of acute kidney injury among children diagnosed with scrub typhus admitted to a tertiary care hospital in Vijayawada and to assess the clinical and laboratory characteristics associated with AKI.

Materials and Methods: A hospital-based observational study was conducted among children aged Children aged 4 to 12 years admitted with confirmed scrub typhus at a tertiary care hospital in Vijayawada. During the period from August 2023-December 2024. Diagnosis was established by IgM ELISA or other standard serological methods. Demographic details, clinical manifestations, laboratory parameters, and outcomes were recorded. Acute kidney injury was defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria. The incidence of AKI and its association with clinical variables were analyzed.

Results: In the present study, 65 children diagnosed with scrub typhus were evaluated to determine the incidence and profile of Acute Kidney Injury (AKI). The highest proportion of children belonged to the 7–9 years age group (49.2%), with a slight male predominance (53.8%). AKI was documented in 13.8% of children. Interestingly, younger children (4–6 years) accounted for the highest proportion (44.4%) of AKI cases, although the association with age was not statistically significant (p=0.155). The occurrence of AKI was significantly higher in males (88.9% of AKI cases) compared to females, a finding that was statistically significant (p=0.023). The majority of AKI cases were classified as Stage 3 (77.8%) per KDIGO guidelines, reflecting severe renal impairment. Serum creatinine levels increased proportionately with the severity of AKI, with Stage 3 patients showing the highest mean levels (2.8 ± 0.0 mg/dL). Younger children (4–6 years) had the highest average serum creatinine levels among AKI cases. Urine output was significantly reduced in children with AKI (0.4 ± 0.10 ml/kg/hr) compared to those without AKI (1.26 ± 0.2 ml/kg/hr), with a highly significant p-value (<0.001).Complications such as encephalopathy (22.2%), ARDS (11.1%), and shock (11.1%) were notably more frequent among AKI patients. Moreover, a statistically significant association was observed between AKI and the development of Multi-Organ

Dysfunction Syndrome (MODS), with 100% of MODS cases found among the AKI group (p=0.001). Dialysis was required in 44.4% of AKI patients, while none of the non-AKI patients required renal replacement therapy. Mortality was recorded only in the AKI group (11.1%), further emphasizing the clinical severity associated with renal involvement in scrub typhus.

Conclusion: Acute kidney injury is a notable complication of pediatric scrub typhus and is associated with increased disease severity and prolonged hospitalization. Early recognition, prompt diagnosis of scrub typhus, careful monitoring of renal function, and timely management can reduce adverse outcomes. Routine assessment of kidney function should be considered in all children admitted with scrub typhus, particularly those with severe systemic manifestations.

Keywords: Scrub typhus, Acute kidney injury, Children, Pediatric infections, KDIGO, Renal complications, Vijayawada.

INTRODUCTION

Infections account for a significant proportion of community-acquired acute kidney damage (AKI) in India. The often, associated disorders encompass malaria, leptospirosis, dengue, enteric fever, as well as viral and bacterial diseases. Scrub typhus, caused by the rickettsia Orientia tsutsugamushi, is endemic throughout Asia, with an estimated one million cases yearly; yet, it remains significantly underdiagnosed and underreported as a cause of hospitalisation. The World Health Organisation (WHO) recognises scrub typhus as a re-emerging illness in South-East Asia and the South-Western Pacific, with a case fatality rate reaching 30% in untreated cases, and emphasises the necessity for its surveillance.Scrub typhus has been documented in many regions of India and has lately been recognised as a significant neglected zoonosis of public health concern.[1]

Scrub typhus is regarded as a rare aetiology of acute kidney injury, even in endemic regions.Renal involvement is considered a result of multi-organ failure syndrome subsequent to sepsis.This has partly resulted from the inability to achieve an appropriate diagnosis due to the unavailability of diagnostic investigations.Recent investigations indicate an increased frequency of renal involvement in this illness.These investigations, however, have employed either clinical characteristics alone or in conjunction with serology, utilising arbitrary antibody titre cut-offs from single samples to establish a diagnosis.Dependence only on serology is problematic in endemic regions, and the use of nucleic acid-based testing (NAT) is advised.[2]

Acute kidney injury (AKI) represents a significant global health concern, with its incidence notably escalating, impacting approximately 13–18% of hospitalised patients. This condition leads to prolonged hospitalisations, elevated healthcare expenditures, and adverse short-term and long-term outcomes, particularly in individuals with chronic kidney disease (CKD).The incidence of acute kidney injury (AKI) among patients with infectious diseases, particularly those with sepsis, is reported to range from 5% to 51%.Renal involvement in scrub typhus is prevalent, manifesting from mild haematuria or proteinuria, with a frequency of 10–20%, to severe consequences such as acute renal failure, nephrotic syndrome, and end-stage renal disease necessitating long-term haemodialysis. The frequency of acute kidney injury (AKI) in scrub typhus varies between 8% and 40%, depending on the diagnostic criteria applied.The risk factors and prognosis of acute kidney injury linked with scrub typhus have been little researched.[3-6]

Patients with scrub typhus who experience acute kidney injury (AKI), particularly those with comorbidities such as diabetes mellitus (DM), hypertension, and chronic kidney disease (CKD), exhibit a poor prognosis and prolonged hospital stays.

This study aimed to investigate the incidence of acute renal damage as a complication in children with scrub typhus admitted to a tertiary care hospital in Vijayawada.

Aims & Objectives

1. To estimate the incidence of occurrence of AKI as a complication in children aged4-12 years with scrub typhus.
2. To assess the severity of Acute kidney injury among affectedchildren.
3. To assess the correlation between the severity of Acute kidney injury and the severity of scrub typhus in affected children

MATERIALSANDMETHODS

Children aged 4to 12 years presenting with acute febrile illness and confirmed positive for scrub typhus, admitted to the paediatric ward and PICU, are selected. History of symptoms including tiredness, dyspnoea, urinary output, haematuria, and generalised oedema. Subsequently, pertinent examinations, including a renal function test, will be conducted, and hourly urine output will be monitored. Patients with AKI as per KDIGO criteria are evaluated.

RESULTS

Age

It was observed that the majority of the children in the present study belonged to the age group of 7 to 9 years, accounting for 49.2% of the study population. This was followed by 27.7% of children in the 10 to 12 years age group. The lowest numbers of children were in the 4 to 6 years age group, comprising 23.08% of the study population.

Table1: Age wise distribution

Age group (Years)	No.	%
4 - 6	15	23.08
7 – 9	32	49.2
10 – 12	18	27.7
Total	65	100.00

Gender:

Males constituted 53.8% of the study population, whereas females accounted for 46.2%.

Table 3: Gender wise distribution

Age group (Years)	No.	%
Male	35	53.8
Female	30	46.2
Total	65	100.00

Table 4: Age and Gender wise comparison

Age group (Years)	Male	%	Female	%	Total	%
4 - 6	10	28.6	5	14.3	15	23.1
7 – 9	14	40.0	18	51.4	32	49.2
10 – 12	11	31.4	7	20.0	18	27.7
Total	35	100	30	85.7	65	100.0
Chi-square = 2.68 p=0.261 (not significant)						

It was observed that the incidence of Acute Kidney Injury (AKI) among the study participants was 13.8%, with 9 out of 65 children developing AKI. The majority of the children (86.2%) did not develop AKI.

Table 5: Incidence of AKI

AKI	No.	%
Present	9	13.8
Absent	56	86.2
Total	65	100.00

Table 6: Age and AKI wise comparison

	Age group (Years)					AKI
	No	%	Yes	%	Total	%
6-Apr	11	19.6	4	44.4	15	23.1
7 – 9	30	53.6	2	22.2	32	49.2
10 – 12	15	26.8	3	33.3	18	27.7
Total	56	100	9	100	65	100
Chi-square = 3.73 p=0.155 (not significant)						

It was observed that the incidence of AKI was highest in the 4 to 6 years age group, where 44.4% of the affected children belonged to this age group. In comparison, 33.3% of AKI cases were seen in the 10 to 12 years age group, and only 22.2% were in the 7 to 9 years age group. Among children without AKI, the majority were in the 7 to 9 years age group (53.6%), followed by 26.8% in the 10 to 12 years age group and 19.6% in the 4 to 6 years age group. Although a higher proportion of AKI was observed in younger children (4 to 6 years), the association between age and AKI occurrence was not statistically significant (p>0.05).

Table 7: Gender and AKI wise comparision

Age group (Years)	AKI					
	No	%	Yes	%	Total	%
Male	27	48.2	8	88.9	35	53.8
Female	29	51.8	1	11.1	30	46.2
Total	56	100	9	100	65	100
Chi-square = 3.73 p=0.155 (not significant)						

It was observed that the incidence of AKI was significantly higher among male children as compared to females. Among the 9 AKI cases, 88.9% were males and only 11.1% were females. In contrast, among children without AKI, 48.2% were males and 51.8% were females. This difference in AKI occurrence between males and females was found to be statistically significant ($p<0.05$).

KDIGO Criteria

It was observed that among the 9 cases of Acute Kidney Injury (AKI) in children with scrub typhus, the majority of patients had advanced stages of AKI. Stage 1 AKI was not observed in any case (0%). Stage 2 AKI was seen in 2 cases (22.2%), while Stage 3 AKI was noted in 7 cases (77.8%).

Table 8: Staging of AKI based on KDIGO Criteria (n=9)

AKI Stage (KDIGO)	No.	%
Stage 1	0	0.0
Stage 2	2	22.2
Stage 3	7	77.8
Total	9	100.00

Serum Creatinine:

It was observed that the mean serum creatinine levels increased progressively with the severity of AKI stages based on the KDIGO criteria. In Stage 1 AKI, the mean serum creatinine level was 0.9 ± 0.1 mg/dL. In Stage 2, it increased to 1.6 ± 0.2 mg/dL, and the highest serum creatinine level was observed in Stage 3 AKI cases with a mean value of 2.8 ± 0.0 mg/dL.

Table 9: Serum Creatinine Levels in AKI Cases based on KDIGO Criteria

AKI Stage (KDIGO)	No.	Serum Creatinine(Mean ± SD) mg/dL
Stage 1	0	0
Stage 2	2	1.6 ± 0.2
Stage 3	7	2.8 ± 0.0

Table 10: Serum Creatinine Levels based on age in AKI cases

Age group (Years)	No.	Serum Creatinine(Mean ± SD) mg/dL
4 - 6	5	1.09 ± 1.05
7 – 9	3	0.73 ± 0.61
10 – 12	1	0.88 ± 0.77

It was observed that the mean serum creatinine levels were highest in the 4 to 6 years age group (1.09 ± 1.05 mg/dL) among children with AKI. This was followed by the 10 to 12 years age group with a mean serum creatinine level of 0.88 ± 0.77 mg/dL. The lowest mean serum creatinine level was observed in the 7 to 9 years age group (0.73 ± 0.61 mg/dL). Thus, younger children (4 to 6 years) had relatively higher serum creatinine levels in the present study.

Table 11: Urine Output Levels based on AKI

AKI	No.	Urine Output (ml/kg/hr) (Mean ± SD)	T-test	p-value
Yes	9	0.4 ± 0.10	-20.3	0.001*
No	56	1.26 ± 0.2		

It was observed that the mean urine output was significantly lower in children with AKI compared to those without AKI. The mean urine output in AKI cases was 0.4 ± 0.10 ml/kg/hr, whereas in non-AKI cases, it was 1.26 ± 0.2 ml/kg/hr. This difference was found to be highly statistically significant ($p < 0.01$), indicating that reduced urine output was strongly associated with the presence of AKI.

Table 12: Distribution of other complications associated with scrub typhus

Complications			AKI			
	No	%	Yes	%	Total	
ARDS	0	0	1	11.1	1	1.5
Encephalopathy	0	0	2	22.2	2	3.1
Shock	0	0	1	11.1	1	1.5
None	56	100	5	55.6	61	93.8
Total	56	100	9	100	65	100

It was observed that complications were significantly more common among children with AKI compared to those without AKI. Among the AKI group, 22.2% developed encephalopathy, 11.1% developed ARDS, and 11.1% had shock. In contrast, none of the children without AKI developed these complications. The majority of children without AKI (100%) had no complications, whereas only 55.6% of children with AKI remained free of complications.

Table 13: Comparison of isolated AKI and MODS

AKI	MODS					
	Yes	%	No	%	Total	
Present	4	100	5	8.2	9	13.8
Absent	0	0	56	91.8	56	86.2
Total	4	100	61	100	65	100
Fisher's Exact Test p=0.001* (significant)						

In the present study, among the 65 children with scrub typhus, isolated Acute Kidney Injury (AKI) was observed in 9 cases (13.8%). Of these, 4 cases (100%) had associated Multi-Organ Dysfunction Syndrome (MODS), whereas 5 cases (8.2%) had AKI without MODS. Among the 56 cases without AKI, the majority (91.8%) did not develop MODS. The association between AKI and MODS was found to be statistically significant ($p<0.05$).

Table 14: Distribution based on requirement of dialysis in AKI

Dialysis			AKI			
	No	%	Yes	%	Total	
Yes	0	0	4	44.4	4	3.2
No	56	100	5	55.6	61	93.8
Total	56	100	9	100	65	100

t was observed that the requirement of dialysis was significantly higher among children with AKI. In the AKI group, 44.4% of children required dialysis, whereas none of the children without AKI required dialysis. 55.6% of children with AKI recovered without the need for dialysis.

Table 15: Distribution based on severity of Scrub Typhus stage of AKI

Scrub Typhus	Stages 1 & 2	%	Stage 3	%	Total	%
Mild & Moderate	0	0	3	42.9	5	55.6
Severe	2	100	4	57.1	4	44.4
Total	2	100	7	100	9	100
Fisher's Exact Test p=0.50 (Not significant)						

It was observed that among the 9 cases of Acute Kidney Injury (AKI) in children with scrub typhus, none of the patients had Stage 1 AKI. Stage 2 AKI was noted exclusively in 2 cases (100%) with moderate scrub typhus. Stage 3 AKI was more frequently observed, with 3 cases (42.9%) belonging to moderate scrub typhus and 4 cases (57.1%) to severe scrub typhus. However, this association between the severity of scrub typhus and the stage of AKI was not statistically significant ($p>0.05$).

Table 16: Distribution based on outcome and AKI

Died				AKI		
	No	%	Yes	%	Total	
Yes	0	0	1	11.1	1	1.5
No	56	100	8	88.9	64	98.5
Total	56	100	9	100	65	100

It was observed that mortality was noted only among children with AKI. In the AKI group, 11.1% of children expired, whereas there was no mortality in the non-AKI group. All children without AKI (100%) survived, while 88.9% of children with AKI were discharged successfully.

DISCUSSION

Findings of the Present Study

In the present study involving 65 pediatric patients diagnosed with scrub typhus, the age distribution revealed that nearly half of the study population (49.2%) belonged to the 7–9 years age group. This was followed by 27.7% in the 10–12 years category, and the youngest age group of 4–6 years accounted for 23.1% of cases. This distribution suggests a higher vulnerability or detection of scrub typhus in the midchildhood age group, with fewer cases observed among the youngest children. Gender-wise, the study had a slight male predominance, with 53.8% of the participants being male and 46.2% female.

When the interaction between age and gender was analyzed, it was observed that in the 4–6 years age group, male children constituted a greater share (28.6%) compared to females (14.3%). Interestingly, in the 7–9 years age group, the trend reversed, with females (51.4%) outnumbering males (40.0%). In the oldest group (10–12 years), males again showed a higher proportion (31.4%) relative to females (20.0%). However, statistical analysis using the Chi-square test showed that these differences were not significant ($p=0.261$), indicating that age and gender distributions were relatively balanced across the spectrum of the study cohort.

The overall incidence of Acute Kidney Injury (AKI) among the study population was found to be 13.8%,

with 9 out of 65 children developing AKI. The majority of patients (86.2%) did not exhibit any signs of renal involvement. A deeper dive into age-wise distribution of AKI showed that the 4–6 years age group had the highest proportion of affected cases (44.4%), followed by the 10–12 years group (33.3%), and the 7–9 years group (22.2%). Among those without AKI, the majority were in the 7–9 years group (53.6%), reflecting that AKI was relatively more prevalent in the younger age brackets. However, these differences did not reach statistical significance (p=0.155), though they provide a trend worthy of further investigation.

A significant gender-based disparity was found in the occurrence of AKI. Of the 9 children with AKI, 88.9% were males and only 11.1% were females, making the association between gender and AKI statistically significant (p=0.023). This finding underscores the need to further explore the potential gender-related biological or behavioral factors that may predispose male children to a higher risk of kidney involvement in scrub typhus infections.

When AKI cases were staged using the KDIGO criteria, none of the children were found to have Stage 1 AKI. Stage 2 was seen in only 2 cases (22.2%), whereas the vast majority (77.8%) were diagnosed with Stage 3 AKI, indicating a trend toward late presentation or rapid progression of renal complications in scrub typhus. The mean serum creatinine levels corresponded with the severity of AKI stages—Stage 2 had a mean of 1.6 ± 0.2 mg/dL, and Stage 3 had a significantly higher mean of 2.8 ± 0.0 mg/dL, reinforcing the clinical staging criteria.

Analyzing serum creatinine levels in relation to age revealed that the highest values were seen in the youngest group (4–6 years), with a mean of 1.09 ± 1.05 mg/dL. This was followed by the 10–12 years group (0.88 ± 0.77 mg/dL), and the lowest levels were noted in the 7–9 years group (0.73 ± 0.61 mg/dL). This supports the observation that younger children in the present study not only had a higher incidence of AKI but also demonstrated more severe renal impairment as reflected by serum creatinine levels.

Urine output was significantly reduced in children with AKI. The mean urine output in AKI cases was only 0.4 ± 0.10 ml/kg/hr, which was markedly lower than the output in non-AKI children, which averaged 1.26 ± 0.2 ml/kg/hr. The statistical significance of this difference (p<0.001) confirms that reduced urine output was a strong indicator of renal dysfunction among affected children and serves as a key parameter in earlyidentification.

Scrub typhus-related complications were more frequent in children with AKI. Among the 9 AKI cases, 22.2% developed encephalopathy, 11.1% had ARDS, and another 11.1% developed shock. In contrast, none of the children without AKI exhibited any of these serious complications, and all had an uncomplicated course. This marked difference highlights the systemic impact of AKI in scrub typhus and its association with multi-organ involvement.

The relationship between AKI and MODS (Multi-Organ Dysfunction Syndrome) was statistically significant (p=0.001). All 4 children with MODS were from the AKI group, accounting for 100% of MODS cases. Meanwhile, 91.8% of those without AKI did not develop MODS, underscoring the strong correlation between kidney involvement and broader organ dysfunction in the clinical progression of scrub typhus.

The requirement for dialysis among AKI patients further emphasized the severity of renal compromise. Nearly half (44.4%) of the AKI group required dialysis, whereas none of the children without AKI required such intervention. However, it is encouraging to note that 55.6% of AKI patients recovered without dialysis, suggesting variable progression and possibly successful early interventions in some cases.

When comparing the severity of scrub typhus with the stage of AKI, it was found that Stage 2 AKI occurred exclusively in children with moderate scrub typhus, while Stage 3 AKI was observed across both moderate (42.9%) and severe (57.1%) forms. Despite this trend, the association was not statistically significant (p=0.50), which might be due to the small sample size or overlapping clinical presentations.

Regarding patient outcomes, mortality was confined to the AKI group. Out of the 9 children with AKI, one child (11.1%) succumbed to the illness, whereas all 56 children without AKI survived. The survival rate was 100% in the non-AKI group and 88.9% in the AKI group. This clearly indicates that AKI is not only a significant marker of disease severity but also a predictor of mortality in pediatric scrub typhus.

The present study aimed to evaluate the incidence, severity, and clinical implications of Acute Kidney Injury (AKI) in pediatric patients diagnosed with scrub typhus admitted to a tertiary care hospital in Vijayawada. The findings are insightful and merit comparison with similar literature to understand regional trends and global context.

Incidence and Prevalence of AKI

In this study, AKI was observed in 13.8% of the pediatric scrub typhus cases. This incidence aligns with data from other parts of India and neighboring countries. For instance, a study conducted by Varghese et al. in South India reported AKI in 20% of children with scrub typhus, indicating a relatively high renal complication rate in endemic areas. Another significant study from Nepal by Pathak et al., 2019 revealed that 65.8% of children had renal involvement, suggesting a remarkably high incidence, possibly due to late presentation, delayed diagnosis, or differences in population susceptibility.[7,8]

In contrast, a recent Eastern India study by Kumar Jana et al., 2023 observed only 2.91% AKI cases among 206 children, likely due to early detection and initiation of therapy, highlighting the role of

timely intervention in reducing renal complications. A study by Kumar Bhat et al., 2014. also reported an AKI incidence of 20%, very similar to the current study findings.[9,10]

Thus, while the present study's incidence lies on the lower side compared to some regions, it remains within the expected range reported across endemic areas.

Severity and Staging Based on KDIGO Criteria

A critical aspect highlighted in the present study is the severity of AKI, with 77.8% of the cases classified as Stage 3 using the KDIGO criteria. None of the patients presented with Stage 1 AKI. This finding suggests either a rapid progression of renal injury or delay in diagnosis. Similarly, Chaudhary et al. (Nepal) observed high creatinine levels and renal compromise in over 65% of their pediatric cohort, with many requiring intensive care.[8]

The high frequency of severe AKI (Stage 3) also parallels findings from Attur et al., 2013. who noted that late hospital presentations often result in advanced renal failure and systemic complications. Therefore, these observations collectively stress the importance of early recognition and renal function monitoring in all scrub typhus cases.[11]

Clinical and Laboratory Correlates: Serum Creatinine and Urine Output

The present study documented significantly elevated serum creatinine levels, especially in Stage 3 AKI (2.8 ± 0.0 mg/dL), and significantly reduced urine output (0.4 ± 0.10 ml/kg/hr) compared to non-AKI children (1.26 ± 0.2 ml/kg/hr). This inverse correlation has been widely reported. For instance, Chrispal et al. found similar biochemical patterns in AKI patients with scrub typhus, emphasizing oliguria as a reliable early marker.[12]

Gender and Age-wise Trends

An intriguing observation from the Vijayawada study was the male preponderance in AKI cases (88.9%), which was statistically significant. This aligns with Bhattacharya et al. (2023), where male children represented 68.2% of the scrub typhus cases with complications, including AKI. Some hypothesize that biological differences or higher exposure to environmental vectors among boys may explain this pattern.[13]

In terms of age, children aged 4–6 years showed the highest AKI incidence (44.4%), reinforcing that younger children may be more vulnerable. This trend mirrors that in North Indian studies, where younger children exhibited higher rates of systemic complications, including renal dysfunction.

Associated Complications

The present study noted encephalopathy (22.2%), ARDS (11.1%), and shock (11.1%) in AKI cases, compared to none in non-AKI cases. These complications were also emphasized in studies such as Narayanappa et al., who found multi-organ involvement in over 30% of pediatric scrub typhus cases . Moreover, MODS (Multiorgan dysfunction syndrome) was significantly associated with AKI in the present study (p = 0.001), consistent with findings from Chaudhary et al., who documented multiple complications like myocarditis, hepatitis, and renal failure in patients with MODS.[8,14]

These associations indicate that AKI is both a marker and mediator of disease severity, increasing the risk of further systemic complications.

Dialysis Requirements and Outcomes

Among the 9 AKI cases, 44.4% required dialysis, demonstrating significant renal impairment. This finding is more severe compared to the 4% dialysis requirement in the Attur et al., 2013, possibly reflecting differences in inclusion criteria, severity at presentation, or access to nephrology care.[46] In terms of outcome, mortality was confined to the AKI group (11.1%), while all non-AKI children survived. These findings underscore the prognostic value of AKI in scrub typhus. Similar outcomes were reported by Vikrant et al., 2013 who noted increased mortality in children with AKI and other systemic complications.[7]

Severity of Scrub Typhus and AKI Staging

The study attempted to correlate scrub typhus severity with AKI stage, although no statistical significance was found. However, all Stage 2 AKI cases occurred in moderate disease, and most Stage 3 AKI cases were seen in severe presentations. This is conceptually in line with studies by Chrispal et al., who linkeddisease severity to the progression of organ damage.[12]

Role of Doxycycline Treatment Timing

Early initiation of doxycycline (within 5 days of symptom onset) is strongly associated witha lower incidence of severe complications, including AKI. Delayed initiation (after day 7)is linked to a higher risk of AKI, respiratory failure, encephalitis, and even death. The longer the infection remains untreated, the more systemic inflammation and vascular damage occur. Early doxycycline rapidly suppresses bacterial replication, thus reducinginflammation and endothelial injury that leads to AKI.

Supporting Evidence

Several cohort studies (especially from endemic areas like India, South Korea, and Thailand) have shown that delayed doxycycline is an independent risk factor for AKI. A 2017 Korean study specifically showed that late treatment (>5 days) increased odds of AKI by around 2–3 times compared to early treatment.

Scrub typhus, a mite-borne infectious disease caused by Orientia tsutsugamushi, is increasingly recognized as a significant public health concern in the Asia-Pacific region. Particularly in pediatric populations, scrub typhus presents with a wide spectrum of clinical anifestations ranging from mild febrile illness to life-threatening complications such as Acute Kidney Injury (AKI), encephalopathy, acute respiratory distress syndrome (ARDS), and multi-organ dysfunction syndrome (MODS). The present study undertaken at a tertiary care hospital in Vijayawada offers valuable insights into the

epidemiological characteristics, incidence, and clinical implications of AKI among children diagnosed with scrub typhus.

The incidence of AKI in this study was observed to be 13.8%, consistent with similar studies conducted across various Indian sub-regions. This moderately high incidence underlines the importance of renal involvement as a key determinant of severity in scrub typhus. While scrub typhus typically presents with fever, rash, lymphadenopathy, and hepatosplenomegaly, the presence of AKI significantly alters the prognosis and necessitates more intensive care. Early detection of renal dysfunction is thus crucial in improving clinical outcomes.

The age distribution among the study cohort showed that nearly half of the children (49.2%) belonged to the 7–9 years age group, followed by 27.7% in the 10–12 years group and 23.1% in the 4–6 years group. Interestingly, although the mid-childhood group formed the majority of scrub typhus cases, the highest incidence of AKI was noted among children aged 4–6 years (44.4% of AKI cases). This suggests that younger children may have a higher susceptibility to renal complications, potentially due to underdeveloped renal physiological reserves, heightened inflammatory responses, or delays in seeking healthcare. However, statistical analysis indicated that the relationship between age group and AKI occurrence was not significant ($p > 0.05$), highlighting the multifactorial etiology of AKI in scrub typhus.

In terms of gender distribution, the study revealed a slight male predominance (53.8%) in the overall cohort. Among the children who developed AKI, 88.9% were male and only 11.1% were female, a statistically significant difference ($p = 0.023$). This gender disparity in AKI incidence may reflect biological differences in immune response, higher exposure to outdoor vectors in male children, or social and behavioral determinants influencing disease severity or health-seeking patterns. Male predominance has been consistently reported in other Indian studies on scrub typhus, though the reasons remain speculative.

The staging of AKI using the Kidney Disease Improving Global Outcomes (KDIGO) criteria revealed that the majority of AKI cases (77.8%) were classified as Stage 3, indicating advanced renal injury. Stage 2 AKI was observed in 22.2% of the children, while none presented with Stage 1 AKI. This skewed distribution toward severe AKI stages points to either late recognition or a rapid course of renal deterioration in pediatric scrub typhus. The high prevalence of Stage 3 AKI underscores the urgency of implementing early diagnostic protocols and aggressive management strategies in suspected cases.

The serum creatinine values mirrored the severity of AKI observed in the cohort. Children with Stage 3 AKI had a mean serum creatinine of 2.8 ± 0.0 mg/dL, compared to 1.6 ± 0.2 mg/dL in Stage 2 AKI. Age-wise, the highest creatinine levels were noted in the 4–6 years age group (1.09 ± 1.05 mg/dL), reinforcing the trend that younger children are more prone to severe renal impairment. These findings emphasize the importance of routine renal function testing in pediatric febrile illnesses in endemic regions.

Urine output, a vital clinical parameter in AKI diagnosis, was significantly lower in AKI cases (mean: 0.4 ± 0.10 ml/kg/hr) compared to non-AKI cases (1.26 ± 0.2 ml/kg/hr), with a highly significant p-value (< 0.001). This aligns with standard clinical observations that oliguria is a reliable and early indicator of renal dysfunction. The data also advocate for hourly urine output monitoring as an integral component of inpatient management for scrub typhus.

Complications such as encephalopathy (22.2%), ARDS (11.1%), and shock (11.1%) were markedly more frequent in the AKI group compared to the non-AKI group, where no such complications were noted. This correlation between AKI and systemic complications underscores the critical role renal involvement plays in the overall pathophysiology of scrub typhus. Furthermore, MODS was observed exclusively in children with AKI, further strengthening the association between renal injury and multiorgan failure. These findings suggest that AKI not only reflects disease severity but may also contribute to the progression of other organ system failures.

Nearly half (44.4%) of the children with AKI required dialysis, highlighting the critical care demands and resource implications of severe AKI in pediatric scrub typhus. Dialysis was not required in any non-AKI cases, suggesting a direct relationship between renal failure severity and the need for renal replacement therapy. Despite the high rate of dialysis, a majority (55.6%) of AKI cases recovered without it, indicating that timely supportive care can be effective in reversing renal injury in certain cases.

Mortality in the present study was confined to the AKI group, with an 11.1% death rate among affected children. All children without AKI survived, establishing a direct association between AKI and poor outcomes. The presence of AKI may thus serve as a prognostic marker in pediatric scrub typhus, warranting intensive monitoring and early therapeutic intervention.

The severity of scrub typhus and its correlation with AKI staging was also evaluated. While Stage 2 AKI was observed only in moderate cases and Stage 3 AKI was distributed across both moderate and severe cases, the association did not reach statistical significance. Nevertheless, this trend suggests that more severe systemic illness may predispose patients to higher grades of renal injury.

Overall, the findings from this study highlight the significant burden of AKI in pediatric scrub typhus and its association with increased morbidity, complications, and healthcare needs. The results are

consistent with published literature from other parts of India and neighboring countries, which also report high rates of AKI, systemic complications, and mortality in children with scrub typhus.

The study's strengths lie in its focused objective, use of standardized AKI staging criteria, and comprehensive evaluation of demographic, clinical, and biochemical variables. However, limitations such as the relatively small sample size, single-center design, and lack of long-term follow-up data restrict the generalizability of results. Future research should aim at multicentric studies with larger cohorts, incorporation of newer biomarkers of renal injury, and longitudinal tracking of renal recovery postdischarge.

From a clinical perspective, the study underscores the need for heightened awareness about scrub typhus-related AKI in endemic areas. Early diagnosis through rapid serological testing, prompt initiation of doxycycline or azithromycin, and close monitoring of renal parameters can significantly reduce the risk of adverse outcomes.

Moreover, strengthening pediatric critical care infrastructure, including availability of dialysis services, is essential in managing such complications effectively.

In conclusion, this study adds to the growing body of evidence that AKI is a serious, though potentially preventable, complication of scrub typhus in children. The findings call for early detection protocols, robust referral systems, and capacity building in tertiary care centers to ensure timely management of AKI and associated
complications in pediatric scrub typhus patients.

Limitations

Sample Size Constraints: The study was conducted on a relatively smallcohort of 65 pediatric patients. The limited number of children, especially in the subgroup with AKI (n=9), restricts the statistical power and may limit generalizability to the wider pediatric population.

Single-Center Design: This study was carried out in a single tertiary care hospital, which may limit the external validity. Regional healthcare practices, environmental exposure, and demographics may differ, affecting the incidence and presentation of scrub typhus-related AKI.

Lack of Long-Term Follow-Up: The study focused primarily on acute outcomes during hospitalization. Long-term renal outcomes and the potential for chronic kidney disease (CKD) post-AKI were not assessed.

Uncontrolled Confounding Factors: The study did not comprehensively account for other variables such as nutritional status, pre-existing renal conditions, dehydration, or concurrent infections that might have influenced renal outcomes.

Limited Evaluation of Biomarkers: Only serum creatinine and urine output were used to assess AKI based on KDIGO criteria. Other emerging biomarkers such as NGAL or cystatin C, which could provide early detection of AKI, were not included.

CONCLUSION

The present study highlights that Acute Kidney Injury is a significant and potentially life-threatening complication in pediatric patients suffering from scrub typhus. Although AKI was seen in a relatively small proportion (13.8%) of the total cohort, its presence was closely associated with severe disease manifestations, including MODS, need for dialysis, and mortality. Male gender emerged as a statistically significant risk factor for developing AKI. Most AKI cases presented at Stage 3 severity, underscoring the need for early detection and aggressive management. Reduced urine output and elevated serum creatinine served as critical indicators of renal involvement. The study also revealed that complications like encephalopathy and ARDS were predominantly observed in children with AKI. These findings reinforce the importance of vigilant renal monitoring in children diagnosed with scrub typhus. Given the serious outcomes associated with AKI, early recognition and timely intervention may substantially improve prognosis. Future studies with larger, multicentric cohorts and long-term follow-up are needed to better understand the predictors, pathophysiology, and recovery patterns of AKI in this setting. The findings from the present study are largely in concordance with regional and international literature, highlighting AKI as a frequent and serious complication in pediatric scrub typhus. While incidence rates vary, the association between AKI and worse outcomes—such as MODS, dialysis, and death—is universally observed Early detection, consistent use of KDIGO criteria for staging, and aggressive supportive management including dialysis, when necessary, remain vital. Further multicentric prospective studies are warranted to standardize management protocols and identify predictors for renal involvement in pediatric scrub typhus.

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