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Research Article

A CROSS-SECTIONAL STUDY TO EVALUATE ACUTE KIDNEY INJURY IN SCRUB TYPHUS PATIENTS

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ABSTRACT

Objective: This study was conducted with the objective to estimate the incidence and severity of acute kidney injury (AKI) scrub typhus patients.

Methods: This was a cross-sectional study conducted 90 patients diagnosed with scrub typhus in a tertiary care center. Basic demographic and treatment details of the patients were recorded. Routine hematological investigations and biochemical profiles were performed upon admission and follow-up. AKI was defined and classified based on the RIFLE criteria.

Results: Mean age of the patients was 49.0±19.5 years and female preponderance was observed. The hemoglobin level was significantly lower in AKI patients as compared to non-AKI patients. Meanwhile, there was a significant increase in mean TLC count, CRP, total bilirubin in AKI patients as compared to non-AKI patients. was significantly higher as compared to those without AKI. Increasing age, ICU admission, shock, urinary abnormalities, and mechanical ventilation were the factors significantly associated with AKI.

Conclusion: AKI is a frequently reported complication in scrub typhus patients. In evaluating febrile illness associated with AKI, scrub typhus should be considered.

Keywords: Acute kidney injury, Scrub typhus, RIFLE criteria.

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INTRODUCTION

In India, scrub typhus is the most commonly reported rickettsial infection. In recent years, an increasing trend is noted in the reported number of scrub typhus patients in India, and scrub typhus is a chief cause for the development of severe acute febrile illness. The complications of scrub typhus include acute renal injury, meningoencephalitis, acute respiratory distress syndrome, hepatitis, and disseminated intravascular coagulation [1].

Renal involvement is the most observed clinical features in scrub typhus patients, with prevalence ranging from 10% to 60% [2]. The renal involvement is often due to multifactorial etiopathogenetic mechanism and can manifest as subtle urinary abnormalities including proteinuria and granular casts to acute kidney injury (AKI) requiring renal replacement therapies. The development of AKI is mainly due to the failure of various organs as result of sepsis in scrub typhus patients. The other causes of AKI are mediated by pre-renal failure, vascular damage, interstitial nephritis, and infections of renal parenchyma. In early days, AKI is a rare event, but in recent years the incidence is reported to be increased in scrub typhus patients [2]. AKI in scrub typhus patients is associated with increasing health-care costs, hospital stay and often have a poor prognosis. The severity of AKI in patients with scrub typhus and the factors associated is poorly studied. This study was conducted with the objective to estimate the incidence of AKI in patients diagnosed with scrub typhus and to assess the severity of AKI.

METHODS

Study settings and patients

This was a hospital-based, analytical, and cross-sectional study conducted in a VIMSAR Medical College, Burla, and Odisha between November 2019 and October 2021.

Inclusion criteria

Patients admitted with acute febrile illness and diagnosed with scrub typhus by positive IgM rapid test were included in the study.

Exclusion criteria

Patients with pre-existing kidney disease, hypertension and diabetes were excluded from the study.

Sample size estimation

Sample size of 90 was calculated at 95% confidence interval to verify an expected 35.8% proportion of scrub typhus patients developing AKI as reported a previous study [2] and taking 10% absolute allowable error. A non-probability and consecutive sampling technique was used and eligible participants with age more than 15, with acute febrile illness with or without eschar and positive rapid IgM slide test were included consecutively in the study till sample size was achieved.

The study has been approved by the Institutional Ethics committee and a written informed consent has been optioned from all participants before enrollment into the study.

Clinical features/variables

After recruitment, basic demographic and treatment details of the patients were recorded. A thorough physical investigation was done in all the patients to detect the presence of eschar, hepato-splenomegaly, lymphadenopathy, rash, etc. Hematological and biochemical investigations were performed during admit and further follow-ups. Urine samples were collected for the estimation of albumin and sugar, as well as for microscopic analysis. A 24 h urine output and serum creatinine levels was monitored regularly. AKI was defined and classified based on the RIFLE criteria [3]. All the complications observed during the study was noted and managed appropriately.

Statistical analysis

The data were expressed as mean±SD and the comparison of variables between patients with AKI and without AKI were done using unpaired student t-test. p<0.05 was considered as significant.

RESULTS

Table 1 describes the baseline demographic features of the study population. Mean age of the scrub typhus patients was 49.0±19.5 years and majority of them (24.4%) were in the 40–54 age group. Females constituted 58.9% of the total subjects and remaining were males 41.1%. Prevalence of AKI among scrub typhus patients in our study was 34.4%. Among scrub typhus patients who developed AKI, stage 1 AKI was most common (67.7%), followed by stage 2 AKI (29%) and only one (3.3%) patient had stage 3 AKI.

Table 2 describes the analysis of the hematological and bio-chemical parameters associated with AKI. The mean hemoglobin level of patients who developed AKI was significantly (p=0.030) lower (11.68±2.30 g/dL) as compared to those without AKI (12.73±2.07 g/dL), whereas the mean TLC count of patients who developed AKI was significantly higher (10.74±4.20×10^3/dL) as compared to those without AKI (7.53±2.90×10^3/dL).

The mean platelet count of patients with AKI was slightly lower (325.65±146.83×10^3/dL) as compared to those without AKI (336.58±138.91×10^3/dL). This difference was however not found to be statistically significant (p>0.05).

The mean total bilirubin level among patients who developed AKI was significantly higher (1.37±0.67 mg/dL) as compared to those without AKI (0.64±0.37 mg/dL). The mean CRP level among patients with AKI was also significantly higher (11.44±4.83 mg/dL) as compared to those without AKI (5.97±2.99 mg/dL).The mean creatinine and urea level among cases with developed AKI was significantly higher was found to be comparable to that cases without AKI.

Table 3 describes factors linked with AKI. Prevalence of AKI among scrub typhus seems to be highest among older age patients aged 60 years or more (48.4%). This difference in incidence of AKI with increasing age was statistically significant (p<0.001). Incidence of AKI was slightly higher among male scrub typhus patients (35.1%), as compared to female patients (34%), the observed alterations were however not found to be statistically significant (p>0.05). Rural-urban difference in the incidence of AKI was also found not statistically significant.

Overall, shock occurred in 9 (10%) of patients with scrub typhus. Significant association was seen in presence of shock and AKI (p=0.031). Overall, hemodialysis was required in 4 (4.4%) of patients with scrub typhus. Dialysis requirement was more in scrub typhus patients with AKI (12.9%) as compared to those who did not had AKI (0%). Significant association was seen in hemodialysis requirement and AKI (p=0.012). Oliguria occurred in 28 (31.1%) of cases with scrub typhus. Significant pyuria observed in 5 (5.6%) of cases with scrub typhus, also hematuria occurred with 12 cases (13.3%) scrub typhus. Proteinuria occurred in 23 (25.6%) of patients with scrub typhus. Significant association was seen with oliguria, pyuria, hematuria, and protein uria with AKI. ICU admission was required in 13 cases (14.4%) with scrub typhus. Number of ICU admissions were more in scrub typhus cases along with AKI (32.3%) as associated to those cases who did not reported AKI (5.1%). Significant association was seen in requirement of ICU admission and AKI (p=0.002). Mechanical ventilation was required in 13 (14.4%) of patients with scrub typhus.

Table 1: Baseline characteristics of the patients

Variables	Values (*n*=90), (*n*,%)
Age in years (Mean±SD)	49.0±19.5
Gender	
Male	37 (41.1)
Female	*53 (58.9)*
AKI	
Present	31 (34.4)
Absent	59 (65.6)
Stages of AKI (n=31)	
Stage 1	21 (67.1)
Stage 2	9 (29.0)
Stage 3	1 (3.3)

AKI: Acute kidney injury

Table 2: Analysis of hematological and bio-chemical parameters associated with AKI

Biochemical parameters (Mean±SD)	Acute kidney injury		p-value
	Yes	No	
Hb	11.68±2.30	12.73±2.07	0.030
TLC	10.74±4.20	7.53±2.90	<0.001
Platelet count	325.65±146.83	336.58±138.91	0.722
Total bilirubin	1.37±0.67	0.64±0.37	<0.001
CRP	11.44±4.83	5.97±2.99	<0.001
Creatinine	2.09±0.75	0.88±0.42	<0.001
Urea	64±15.72	28.05±11	<0.001

Table 3: Analysis of the factors associated with acute kidney injury

Variable	Acute kidney injury		Total	p-value
	Yes	No		
Age group (years)				0.048
<30	1 (6.3)	15 (93.8)	16	
30–44	7 (31.8)	15 (68.2)	22	
36–59	8 (38.1)	13 (61.9)	21	
60 and above	15 (48.4)	16 (51.6)	31	
Gender				0.912
Female	18 (34.0)	32 (66.0)	53	
Male	13 (35.1)	24 (64.9)	37	
Residence				
Rural	14 (32.6)	29 (67.4)	43	0.890
Urban	17 (36.2)	30 (63.8)	47	
Shock				
Yes	7 (22.6)	3 (5.1)	9	0.031
No	24 (77.4)	56 (94.9)	81	
Hemodialysis				0.012
Yes	4 (12.9)	0 (0.0)	4	
No	27 (87.1)	59 (100.0)	86	
Oliguria				
Yes	19 (61.3)	9 (15.3)	28	<0.001
No	12 (38.7)	50 (84.7)	62	
Significant pyuria				
Yes	5 (16.1)	0 (0.0)	5	0.004
No	26 (83.9)	59 (100.0)	85	
Hematuria				
Yes	8 (25.8)	4 (6.8)	12	
No	23 (74.2)	55 (93.2)	78	
Proteinuria				
Yes	14 (45.2)	9 (15.3)	23	0.005
No	17 (54.8)	50 (84.7)	67	
ICU admission				
Yes	10 (32.3)	3 (5.1)	13	0.002
No	21 (67.7)	56 (94.9)	77	
Mechanical ventilation				
Yes	10 (32.3)	3 (5.1)	13	0.002
No	21 (67.7)	56 (94.9)	77	
Mortality				
Yes	3 (9.7)	1 (1.7)	4	0.116
No	28 (90.3)	58 (98.3)	86	
Total	31 (34.4%)	59 (65.6%)	90	

Overall mortality happened in 4 (4.4%) cases diagnosed with scrub typhus. Mortality rate observed further in scrub typhus patients who developed AKI cases (9.7%) as compared to those who did not had AKI patients (1.7%). The observed changes were however not established to be statistically significant (p>0.05).

DISCUSSION

The present study was performed to report the frequency of AKI patients those who also diagnosed along with scrub typhus and assessing its severity among AKI using RIFLE criteria.

Our study findings revealed that scrub typhus patients mean age was 49.0±19.5 years. Jayaprakash *et al*. [4] similar to present study found that the average age of the patients diagnosed with scrub typhus was found to be 45.7. However, many previous studies reported that a lower mean age in the incidence of scrub typhus. Kumar *et al*. [5] found that average age of the scrub typhus cases was found to be34.16. Gaba *et al*. [6] reported that the mean age at the time of diagnosis of scrubtyphus cases was found to be 32.3±13. A study carried out in SriLanka [7] also found that the mean age of scrub typhus cases was reported as 34.6. A hospital based study in Andhra Pradesh [8] reported that most of the scrub typhus cases belonging to the age group was found to be 11–30 years (41%). Vikrant *et al.* [9] similarly observed that the average of the scrub typhus cases in a tertiary care center was found to be 41.4±15.9 years.

Majority of the study participants in the present study were females (58.9%). A similar female majority has been reported in previous studies [7-10]. However, male preponderance also been reported in few studies [5,6,11].

In this study, among scrub typhus patients, 34.4% of them developed AKI and majority of them were in stage 1 AKD. Kumar *et al*. [11] also observed AKI among in 35.3% of the patients [40] However, different studies have reported varying level of incidence of AKD in scrub typhus patients. Attur *et al*. [10] observed that 23.2 % patients had AKI. However, a study carried out in India, [5] reported that renal deformities were observed with nearly 82% of cases who showed the indications of AKI in 53%. In a study carried out in South India, Grover and Mehalingam [12] found that about 13.16% of the patients with scrub typhus developed AKI.
AKI in scrub typhus patients is frequently associated with multifactorial origin and is often considered due to multi-organ dysfunctional syndrome which occurs in severe disease.

The most common reported pathology for the AKI are hypovolemia or shock causing impaired renal perfusion, vasculitis, rhabdomyolysis, acute interstitial nephritis, thrombotic microangiopathy, disseminated intravascular coagulation, rhabdomyolysis, and acute tubular necrosis [13].

Incidence of AKI was highest among patients older age patients aged 60 years or more. The alteration in the incidence of AKI with increasing age showed a statistically significant effect. However, a previous study reported that the patient's age was not related to the renal outcome [14].

Our studies has reported a statistically significant difference in the mean hemoglobin level, TLC count, and mean platelet count of cases those established AKI as associated to the cases without AKI. A similar trend has been reported in quite a few previous studies [11,14,15].

Proteinuria, hematuria, pyuria, and granular casts were the most commonly seen urinary abnormalities in patients with scrub typhus and their incidence ranges from 50 to 80%.The mean total bilirubin level among cases who established AKI was significantly higher as associated to the patients without AKI. Kumar *et al*. [5] similarly reported that the hyperbilirubinemia was significantly concomitant with AKI.

In the present study, the overall mortality was seen with 4.4% of patients with scrub typhus. Kumar *et al*. [5] also reported a similar mortality rate. However, a study reported in a tertiary care center in North India [14] reported high mortality in (21.56%) cases, and it was significantly greater in patients with AKI (44.4%). Increased mortality rate reported in AKI cases might be an indication of severity of the disorder.

Since this study was carried out in a single center using a non-probability sampling techniques, there were some limitations in generalizing the study findings.

CONCLUSION

AKI stays the frequently reported impediment in scrub typhus patients. In evaluating febrile illness associated with AKI, scrub typhus should be considered. A wide range of renal association occurs in scrub typhus, since urinary defects to AKI. Increasing age, ICU admission, shock, urinary abnormalities, and mechanical ventilation were the factors significantly associated with AKI.

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