

Renal Dysfunction in Rickettsial Illness

Ritin Sharma¹, Roshan Lal^{2*}, Sanjay Mahajan³, Satish Chaudhary⁴^{1,2,4}Resident, Department of Medicine, IGMC, Shimla, Himachal Pradesh-171001, India³Associate Professor, Department of Medicine, IGMC, Shimla, Himachal Pradesh-171001, IndiaDOI: [10.36347/sjams.2019.v07i07.064](https://doi.org/10.36347/sjams.2019.v07i07.064)

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*Corresponding author: Roshan Lal

Abstract

Original Research Article

Aims: To study renal dysfunction in rickettsial illness (scrub typhus). **Material and Methods:** This was a prospective observational study. Patients aged 18 to 60 years with positive IgM ELISA for scrub typhus with or without eschar were included. The clinical profile was observed. Those having renal dysfunction were analyzed on basis of BUN to creatinine ratio (BCR). **Observations:** Total 151 patients were included in the study, 39 males and 112 females. Renal dysfunction was present in 77(50.1%) patients, 71.4% having BCR > 20, 28.6% having <20. There were 10 deaths, all having raised BCR (p 0.032). **Conclusion:** Renal dysfunction occurs in significant number of patients with scrub typhus. If BCR is used to ascertain possible etiology, prerenal dysfunction is most likely etiology. Patients with raised BCR have higher mortality.

Keywords: Renal Dysfunction, Rickettsial Illness, creatinine ratio.

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INTRODUCTION

Scrub typhus also known as tsutsugamushi disease is a vector born disease transmitted by the bite of larval stage of trombiculid mite and caused by *Orientia tsutsugamusi* [1]. Scrub typhus is endemic to a part of world known as the “tsutsugamushi triangle” which extends from northern Japan and far-eastern Russia in the north, to northern Australia in the south, and to Pakistan and Afghanistan in the west [2]. Scrub typhus often presents with fever, maculopapular rash with an eschar at mite-bite site, myalgia, hepatosplenomegaly and, in severe cases, with acute lung injury, acute kidney injury (AKI), and multi-organ dysfunction [3]. Treatment with doxycycline is associated with a rapid abatement of fever and this effect has even been considered almost diagnostic. Azithromycin is also effective and is easier to administer, given its shorter treatment duration, and less gastrointestinal side effects. It is suitable for use in pregnancy and for children [4].

METHODOLOGY

This was a prospective observational study. All the patients aged 18 to 60 years admitted with febrile illness with positive IgM ELISA for scrub typhus with or without eschar were included in the study. A brief history regarding presenting complaints, relevant past history, and personal history was recorded.

Patients were subjected to general and systemic examination. Hematological and biochemical investigations were done as a part of fever workup. Patients were subjected to imaging studies where indicated. IgM scrub typhus was done by kit method manufactured by InBios International, Inc. This was qualitative ELISA for the detection of IgM antibodies to *O. tsutsugamushi* in serum.

Those having renal dysfunction (BUN >20 or creatinine >1.5, not previously diagnosed as having renal disease) were divided into two subgroups, one having BUN : creatinine ratio > 20 and other group having ratio <20. Statistical analysis was done using EPI info 7.1.5 (Centre Of Disease Control And Prevention, Atlanta, GA, USA). The study was cleared by Institutional Ethics Committee.

OBSERVATIONS

This study was conducted in patients of age group 18-60 years. Total 151 participants were included in the study, 39 were men and 112 patients were women. Nearly 3/4th of patients were females. Geographic distribution of cases was recorded, 38% of cases were from Shimla. Bilaspur and Mandi constituted 15.2% and 13.9% respectively (Table 1). High grade fever was present in 25.2% of patients. Nearly 82% patients reported chills or rigors. Cough

and vomiting were reported by 1/3rd patients. Altered sensorium was present in 17.2% patients. Eschar, a rash/scar which is considered diagnostic of disease was present in 28 patients (18.5%). Lymphadenopathy was present in 15.2% patients. Hepatomegaly, splenomegaly and hepatosplenomegaly was present in 5.3%, 9.9% and 3.9% patients respectively (Table 2).

Leucocytosis and leucopenia were present in 34.4% and 10.6% patients respectively. Thrombocytopenia was present in nearly 70% patients. Raised urea was present in 50.3% (71.8 % male vs 42.9% female, p 0.002) and raised creatinine in 29.8% patients (41.0% males vs 25.9% females, p 0.075). Number of patients having renal dysfunction was significantly more in males. Hyponatremia and hypernatremia was present in 30.5% and 12.6% patients respectively. Hypokalemia and hyperkalemia were

present in 22.5% and 3.3% patients respectively. Hypoalbuminemia was present in 80.8% patients (Table 3).

Renal dysfunction was present in 77 patients (50.8%), 71.4% were having raised BUN: Creatinine ratio vs 28.6% having ratio less than 20:1. Among male patients 75% were having BUN:Creatinine >20 :1, 25% were having ratio <20:1. Among patients admitted to ICU 71.4% were having renal dysfunction, those having renal dysfunction 80% were having BUN:Creatinine ratio>20 suggesting prerenal etiology. Mortality occurred in 10 patients (6.6%), all were having renal dysfunction, out of them 7(70%) were having BUN : Creatinine ratio >20, 3(30%) were having ratio <20. (Table 4) Among all subgroups, those having renal dysfunction majority were having BUN : Creatinine > 20.

Table-1: Geographic distribution of cases

District	All participants (n=151)		Men (n=39)		Women (n=112)	
	No.	%	No.	%	No.	%
Shimla	58	38.4	20	51.3	38	33.9
Mandi	23	15.2	5	12.8	18	16.1
Bilaspur	21	13.9	2	5.1	19	16.9
Solan	14	9.3	2	5.1	12	10.7
Kullu	15	9.9	4	10.3	11	9.8
Sirmaur	9	5.9	4	10.3	5	4.5
Hamirpur	8	5.3	1	2.6	7	6.3
Chamba	1	0.7	0	0	1	0.9
Kinnaur	1	0.7	0	0	1	0.9
Kangra	1	0.7	1	2.6	0	0

Table-2: Clinical characteristics among study participants.

Symptoms and signs	All participants (n=151)		Men (n=39)		Women (n=112)		p-value
	No.	%	No.	%	No.	%	
High grade fever ($\geq 102^{\circ}\text{F}$)	38	25.2	10	25.6	28	25.0	0.936
Chills/Rigors	123	81.5	32	82.1	91	81.3	0.897
Headache	53	35.1	17	43.6	36	32.1	0.197
Cough	50	33.1	14	35.9	36	32.1	0.668
Vomiting	50	33.1	12	30.8	38	33.9	0.718
Diarrhoea	22	14.6	7	17.9	15	13.4	0.487
Abdominal Pain	27	17.9	3	7.7	24	21.4	0.054
Seizures	4	2.6	1	2.6	3	2.7	0.969
Altered sensorium	26	17.2	8	20.5	18	16.1	0.527
Jaundice	23	15.2	8	20.5	15	13.4	0.288
Eschar	28	18.5	7	17.9	21	18.8	0.912
Lymphadenopathy	23	15.2	6	15.4	17	15.2	0.975
Splenomegaly	15	9.9	4	10.3	11	9.8	0.938
Hepatomegaly	8	5.3	3	7.7	5	4.5	0.438
Hepato-splenomegaly	6	3.9	3	7.7	3	2.7	0.168
Ascites	3	1.9	0	0	3	2.7	NA

Table-3: Laboratory characteristics among study participants.

Symptoms and signs	All participants (n=151)		Men (n=39)		Women (n=112)		p-value
	No.	%	No.	%	No.	%	
Leukocytosis	52	34.4	18	46.2	34	30.4	0.074
Leucopenia	16	10.6	4	10.3	12	10.7	0.936
Thrombocytopenia	107	70.8	30	76.9	77	68.8	0.333
BUN>20 mg/dl	76	50.3	28	71.8	48	42.9	0.002
Creatinine >1.5 mg/dl	45	29.8	16	41.0	29	25.9	0.075
Hyponatremia	46	30.5	14	35.9	32	28.6	0.392
Hypernatremia	19	12.6	6	15.4	13	11.6	0.540
Hypokalemia	34	22.5	9	23.1	25	22.3	0.923
Hyperkalemia	5	3.3	2	5.1	3	2.7	0.462
Hypoalbuminemia	122	80.8	33	84.6	89	79.5	0.482

Table-4: BUN: creatinine ratio among study groups

Study group	No.	Renal dysfunction		BUN:Creatinine >20		BUN:Creatinine < 20	
		No.	%	No.	%	No.	%
All participants	151	77	50.9	55	71.4	22	28.6
Female	112	49	43.8	34	69.4	15	30.6
Male	39	28	71.8	21	75.0	7	25.0
ICU admission	21	15	71.4	12	80.0	3	20.0
Mortality	10	10	100	7	70.0	3	30.0
Either ICU admission or Mortality	26	20	76.9	14	70.0	6	30.0

DISCUSSION

Total 151 patients confirmed by IgM ELISA were included in the study. There were more female patients as compared to males. This may be due to reason that females work mostly in fields and males are employed at job at various workplaces. Mahajan *et al* in their study noted that more than 2/3rd of patients were female [5]. Headache was present in 35.1% cases, cough and vomiting in 33.1% cases, diarrhea in 14.1% cases. Eschar, which is considered diagnostic of scrub typhus was present in 18.5% patients. Number of patients having eschar was less in our study, it may be due to dark skin of Asian population [6]. Leucocytosis and leucopenia were present in 34.4% and 10.6% patients respectively. Thrombocytopenia was present in nearly 70% patients. Vikrant *et al.* reported leukocytosis in 44.3% and thrombocytopenia in 61.5% of patients. Raised urea was present in 50.3% (71.8% males vs 42.9% females, p 0.002) and raised creatinine in 29.8% patients (41.0% males vs 25.9% females, p 0.075). Vikrant *et al.* in their study on scrub typhus associated acute kidney injury reported acute kidney injury in 35% of patients [7]. In our study males had higher renal dysfunction. Nearly 81% patients had hypoalbuminemia. Vivekanandan *et al.* reported hypoalbuminemia in 87.5% [8]. Those having renal dysfunction were categorized based on BUN to creatinine ratio, 71.4% were having raised BUN: Creatinine ratio vs 28.6% having ratio less than 20:1. Among male patients 75% were having ratio >20, 25% were having ratio <20. Among patients admitted to ICU having renal dysfunction 80% were having ratio >20. These findings suggest that possible etiology for renal

dysfunction in scrub typhus was prerenal azotemia [9]. The pathophysiology for this may be vascular, as vasculitis due to multiplication of organisms in endothelial cells of small vessels occur in gastrointestinal tract [10]. Mortality occurred in 10 patients (6.6%), all were having renal dysfunction, 70% were having ratio >20, 30% were having ratio <20. (Table 4) Among all subgroups, those having renal dysfunction, number of patients having ratio greater than 20 were more. Mortality occurred more in patients having BUN: Creatinine (BCR) >20. Shigehiko *et al.* concluded that higher mortality among patients with raised BCR, however their study doesn't support BCR as a marker of prerenal azotemia [11].

CONCLUSION

Scrub typhus presents with various complications. Renal dysfunction occurs in significant number of patients. Renal dysfunction occurs more commonly in males. If BUN: Creatinine ratio is used to ascertain possible etiology, prerenal renal dysfunction is most likely etiology. Patients with raised BUN: Creatinine ratio have higher mortality.

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