



Research Article

COMPARISON OF CLASSIFICATION CRITERIA FOR SEVERITY IN SCRUB TYPHUS

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ABSTRACT

Aims: To study classification criteria for severity in scrub typhus admitted in a tertiary care hospital.

Material and Methods: 180 patients of scrub typhus were included in the study. Diagnosis was confirmed by IgM ELISA. Baseline characteristics of patients were recorded. Patients were analyzed by severe sepsis and organ dysfunction criteria. Outcomes by two criteria were compared.

Observations: Out of 180 patients, 130 were females (72%). Organ dysfunction was present in 30% of patients, severe sepsis was present in 36% patients. Mortality occurred in 6.7% patients. Relative risk of death was 6.0 in patients having organ dysfunction, compared to 2.4 in patients having severe sepsis.

Conclusion: Scrub typhus is an important cause of mortality. Identifying patients which may develop fatality, early in the disease course can prevent mortality. Organ dysfunction better predicts mortality and fatal outcome increases with worsening dysfunction.

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INTRODUCTION

Scrub typhus is an acute febrile, infectious illness caused by rickettsia *O. tsutsugamushi*. It was first described in detail by Hashimoto from Japan in 1810.¹ The incubation period for symptoms ranges between 6 to 21 days from exposure. Patients may present with sudden fever, chills, headache, backache, profuse sweating, vomiting and enlarged lymph nodes. A macular or maculopapular rash may appear on the trunk, and later it may extend to the arms and the legs. An eschar at the wound site is the single most useful diagnostic clue.²

Himachal Pradesh is a mountainous state in northern India, with the altitude of 350-7000 meters above mean sea level. During the rainy season, areas at lower altitudes experience average temperature between 20 to 35°C which is suitable for the spread of arthropod vector.³

Complications associated with scrub typhus are not uncommon and sometimes prove to be fatal. Common complications associated with scrub typhus are acute kidney injury, hepatic dysfunction, ARDS, meningoencephalitis, myocarditis and septic shock. Effective treatment in the form of doxycycline, azithromycin are available but in spite of that large number of patients develop complications with high mortality mostly because of delayed in the diagnosis and late initiation of specific treatment.⁴ Patients which develop complications or have fatal outcome is highly variable and not well documented in literature. Our study aims to find, which severity criteria better predicts fatal outcome.

METHODS

The study was conducted among all adult (age \geq 18 yrs) patients of scrub typhus admitted to wards of a tertiary care hospital from July 1st 2015 through June 30th 2016.

Inclusion Criteria

1. Patients diagnosed as Scrub typhus with ELISA.
2. Age \geq 18 years.

Exclusion Criteria

Patients of scrub typhus with coinfections were not included.

Operational Definitions

Scrub typhus

A patient showing clinical features consistent with scrub typhus and confirmed by ELISA.

Severe Disease

A case of scrub typhus with criteria fulfilling severe sepsis or evidence of organ dysfunction was defined as severe disease and a case of scrub typhus leading to mortality was defined as a poor outcome.

Severe sepsis

The harmful host response to infection, systemic response to proven or suspected infection, plus some degree of organ hypofunction i.e.

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1. Cardiovascular: Arterial systolic blood pressure ≤ 90 mm Hg or mean arterial pressure ≤ 70 mm Hg that responds to administration of IV fluids.
2. Renal: Urine output < 0.5 ml/kg perhour for 1 hour despite adequate fluid resuscitation.
3. Respiratory: Pao₂/Fio₂ ≤ 250 or, if lung is the only dysfunctional organ, ≤ 200 .
4. Hematologic: Platelet count $< 80,000/\mu\text{l}$ or 50% decrease in platelet count from highest value recorded over previous 3 days.
5. Unexplained metabolic acidosis: pH ≤ 7.30 or base deficit ≥ 5.0 m Eq/L and plasma lactate level > 1.5 time supper limit of normal.

Septic shock

Defined as Sepsis with hypotension (arterial blood pressure < 90 mm Hg systolic) for at least 1 hour despite adequate fluid resuscitation.

Or

Need for vasopressors to maintain systolic blood pressure ≥ 90 mm Hg or mean arterial pressure ≥ 70 mm Hg.⁵

Organ system failure

Neurologic: Glasgow Coma Score < 6 (in absence of sedation)

Cardiovascular:

- Heart rate < 54 beats per min
- Mean arterial blood pressure < 49 mm Hg (systolic blood pressure < 60 mm Hg)
- Ventricular tachycardia, ventricular fibrillation, or both

Pulmonary:

- PaCO₂ > 50 mm Hg (acutely)
- Ventilator or continuous positive airway pressure dependence on the second day of organ dysfunction

Hepatic:

- Jaundice (bilirubin > 6 mg/100 dL)
- Coagulopathy (Prothrombin Time, 4 sec greater than control, in the absence of anticoagulation)

Renal:

- Urine output < 479 mL/24 hr or < 159 mL/8 hr
- Serum BUN > 100 mg/100 dL
- Serum creatinine > 3.5 mg/100 dL

Hematologic:

- White blood count $< 1,000$ cells/ mm³
- Platelets $< 20,000$ platelets/mm³
- Hematocrit $< 20\%$.⁶

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. tsugamushi* in serum. Data was collected from time of admission to discharge / death. We entered data on Microsoft excel spreadsheet and was analyzed using Epi Info 7.1.5 for windows. We did descriptive analysis for baseline characteristics of patients. The study was cleared by Institutional Ethics Committee.

RESULTS

In this study 180 patients were included, 130 were females and 50 were males. Number of female patients were 2.6 times male patients. Nearly 61 % of patients were below the age of 50 years, with peak incidence in the age group of 18-29 years. Among all age groups number of female patients were more as compared to male counterparts. Distribution of cases in different age groups is given in table 1.

Table 1 Distribution of the study population by age and sex

Age group (Years)	All participants (n=180)		Male (n=50)		Female (n=130)	
	No.	%	No.	%	No.	%
18-29	50	27.8	15	30	35	26.9
30-39	32	17.8	9	18	23	17.7
40-49	28	15.6	5	10	23	17.7
50-59	35	19.4	10	20	25	19.2
60-69	26	14.4	9	18	17	13.1
>70	9	5.0	2	4	7	5.4

When organ dysfunction criteria were used to assess severity renal dysfunction was present in 9% of patients. Hepatic dysfunction was present in 11% of patients, 21% patients had altered mental status. Cardiovascular dysfunction was present in 1.1% and hematologic dysfunction was present in 2.2% patients. At least one of the organ dysfunction was present in 60(30.3%) patients.

Table 2 Distribution of severe scrub typhus cases by organ dysfunction criteria

Organ dysfunction	All participants (n=180)		Men (n=50)		Women (n=130)		p-value
	No.	%	No.	%	No.	%	
Renal							
BUN > 100 mg/dL	6	3.3	1	2.0	5	3.8	0.467
Creatinine > 3.5 mg/dL	17	9.4	3	6.0	14	10.8	0.250
Hepatic							
Hepatic	19	10.6	4	8.0	15	11.5	0.489
Neurologic	38	21.0	11	22.0	27	20.8	0.856
Cardiovascular							
Bradycardia	2	1.1	1	2.0	1	0.0	0.480
Systolic hypotension	1	0.6	1	2.0	0	0.0	0.278
Haematologic	4	2.2	0	57.1	4	3.1	0.269
Anyone of above	60	30.3	16	32.0	44	33.8	0.814

Applying sepsis criteria for severe disease SIRS was present in 63.3% of patients, out of components of SIRS hyperthermia and tachycardia were present nearly 67% of patients. Severe sepsis was present in 36% of patients, 52% males and 30% females (p 0.006).

Both severe sepsis and organ dysfunction was present in 17 (9.4%) patients. However when either of these criteria were used to classify severity 108(60%) patients had severe disease. There were 12(6.7%) deaths.

There were 7 deaths in patients having severe sepsis, and 5 deaths in those who were not having severe sepsis. In patients having organ dysfunction there were 9 deaths and 3 deaths in those not having organ dysfunction. Relative risk of death in severe sepsis group was 2.4 (CI 0.8-7.5, p 0.108), however relative risk of death, when using organ dysfunction criteria was 6.0 (CI 1.7-21.4, p 0.005).

Table 4 Distribution of severe scrub typhus cases by Severe Sepsis criteria

Risk factor	All participants (n=180)		Men (n=50)		Women (n=130)		p-value
	No.	%	No.	%	No.	%	
Component of SIRS							
Hyperthermia	121	67.2	34	68.0	87	66.9	0.890
Hypothermia	0	0.0	0	0.0	0	0.0	NA
Tachycardia	120	66.7	41	82	79	60.8	0.007
Leucocytosis	51	28.3	33	66.0	96	73.8	0.295
Leucopenia	16	8.9	4	8.0	12	9.2	0.528
SIRS	114	63.3	41	82.0	73	56.2	0.001
Severe Sepsis Components							
Cardiovascular	41	22.8	8	16.0	33	25.4	0.179
Respiratory	19	10.6	4	8.0	15	11.5	0.489
Hematologic	78	43.3	18	36.0	60	46.2	0.218
Severe Sepsis	65	36.1	26	52.0	39	30.0	0.006

Table 5 Distribution of severe cases by different criteria

Severity criteria	All participants (n=180)		Men (n=50)		Women (n=130)		p-value
	No.	%	No.	%	No.	%	
Organ dysfunction	60	30.3	16	32.0	44	33.8	0.814
Severe Sepsis	65	36.1	26	52.0	39	30.0	0.006
Both Organ dysfunction and Severe Sepsis	17	9.4	5	10.0	12	9.2	0.874
Either Organ dysfunction or Severe Sepsis	108	60.0	37	74.0	71	54.6	0.017
Death	12	6.7	4	8.0	8	6.2	0.656

Table 6 Comparison of mortality by both criteria

Criteria	No.	Deaths	Relative risk	Confidence interval	P value
Severe sepsis	Present	65	7	2.4	0.8-7.5
	Not Present	115	5		
Organ dysfunction	Present	60	9	6.0	1.7-21.4
	Not Present	120	3		

DISCUSSION

We observed total 180 patients confirmed by IgM ELISA for scrub typhus. In our study the age group mostly affected was 18-29 years. People in this age group are involved in outdoor activities such as agriculture, travel for daily work etc. Mahajan *et al* in their study in western himalyas reported that more than 2/3rd of patients were below 50 years of age.⁷ In our study nearly 72% of patients were females, this higher incidence may be associated, with conventional working in himachal where females actively participate in the farming work and tend to work in a squatting position, whereas males work at some factory or other non agricultural work. Sharma *et al* reported higher incidence among females.⁸

Organ dysfunction was present in patients in form of renal dysfunction, hepatic dysfunction, neurologic dysfunction, cardiovascular and hematologic complications. These were present singly or combination of two or more, those patients were labeled as having MODS. Organ dysfunction was present in 30% patients. Vikrant *et al* reported multiorgan failure in 10.3% patients.⁹ In our study raised creatinine was present in 9.4% of patients. Neurologic dysfunction in form of altered mental state was present in 21% of patients.

In our study SIRS was present in 63% patients (82% males vs 56% females, p 0.001) and severe sepsis in 36% patients (52% males vs 30% females, p 0.006) both common in males.

Incidence of septic shock in scrub typhus varies in literature. Vikrant *et al* reported septic shock in 3% of patients however Kumar *et al* reported septic shock in 22% of patients.^{9,10}

Number of patients having both severe sepsis and organ dysfunction were 17 (9.4%), however when either of these criteria were used 108(60%) patients had severe disease. In our study there were 12(6.7%) deaths, 4 were males and 8 were females. Varghese *et al* reported 9% mortality in their study.¹¹ There were 7 deaths in patients having severe sepsis and 9 deaths in patients having organ dysfunction. Comparing number of deaths using different severity criteria, relative risk of death using severe sepsis criteria was 2.4 (p 0.108), however using organ dysfunction criteria relative risk of death was 6(p 0.005).

CONCLUSION

These findings show that organ dysfunction criteria correlated well with mortality. Organ dysfunction criteria were more stringent than severe sepsis criteria. This suggests that organ dysfunction better predicts mortality and fatal outcome increases with worsening dysfunction. These patients require hospital admission for better care and ICU admission for worsening dysfunction.

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