

Research Article

An Analysis of Clinical Profile and Outcome in Scrub Typhus Patients Requiring Intensive Care Management in a Tertiary Care Hospital

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Abstract: Introduction: Scrub typhus is a zoonotic disease caused by rickettsia *Orientia tsutsugamushi*. It is characterised by acute febrile illness with multiorgan dysfunction. Crop fields are the main reservoir for transmission hence infected when accidentally exposed to mite infested areas. In the pre-antibiotic era scrub typhus was considered as a lethal disease and continues to be major health problem in south Asia and west Pacific regions. Mortality of Scrub typhus ranges from 7% to 30% next to malaria among infectious diseases. **Methods:** All patients had a full work up for fever that included three smears for malarial parasites, serology for dengue, leptospirosis, scrub typhus, enteric fever, blood, urine, sputum or endotracheal cultures and other tests as clinically indicated. A diagnosis of scrub typhus was made when a patient is tested positive for IgM ELISA and other causes of fever excluded. **Results:** total patients, the vasopressor requirements being Dopamine (7%), Nor adrenaline (12.7%) and Vasopressin (2.8%). 1.4% received packed red blood cell transfusions whereas 16.9% had platelet transfusions. 40.8% required non invasive ventilation whereas 8.5% required invasive mechanical ventilation and 1.4% required both non invasive and invasive mechanical ventilation. 1.4% of patients required haemodialysis. The mean duration of ICU and hospital stay were 4.56 and 6.98 days respectively. In hospital mortality was 1.4%. **Conclusion:** In our study we hereby conclude that the incidence of organ dysfunction is highly variable compared with other studies whereas the in hospital mortality was relatively low.

Keywords: Scrub typhus, organ dysfunction, outcome, ICU.

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INTRODUCTION

Scrub typhus is a zoonotic disease caused by rickettsia *Orientia tsutsugamushi*. It is characterised by acute febrile illness with multiorgan dysfunction. Crop fields are the main reservoir for transmission hence infected when accidentally exposed to mite infested areas (Vivekanandan, M. *et al.*, 2010). In the pre-antibiotic era scrub typhus was considered as a lethal disease and continues to be major health problem in south Asia and west Pacific regions (Kweon, S. S. *et al.*, 2009). Mortality of Scrub typhus ranges from 7% to 30% next to malaria among infectious diseases (Kim, D. M. *et al.*, 2010). Recent studies have described scrub typhus as important cause of acute undifferentiated fever in India (Chrispal, A. *et al.*, 2010). The clinical spectrum ranges from subclinical presentation to multiorgan dysfunction and death (Rathi, N. B. *et al.*, 2011). The disease usually

presents with fever, diffuse lymphadenopathy, myalgia, rash, jaundice, thrombocytopenia, capillary leak syndrome, hepatomegaly, and splenomegaly (Sankhyani, N. *et al.*, 2014). The pathognomonic feature of scrub typhus is the necrotic eschar at the bite site.

METHODS

All patients admitted to the multidisciplinary ICU of a tertiary care hospital in South India with acute febrile illness over a one year period (January 1st 2018 to January 1st 2019) were analysed retrospectively.

All patients had a full work up for fever that included three smears for malarial parasites, serology for dengue, leptospirosis, scrub typhus, enteric fever, blood, urine, sputum or endotracheal cultures and other tests as clinically indicated. A diagnosis of scrub typhus was made when a patient is tested positive for IgM

ELISA and other causes of fever excluded. Patients were treated with Ceftriaxone along with enteral doxycycline and intravenous azithromycin as needed.

Organ support was provided to patients depending upon the organ dysfunction. Respiratory support includes non-invasive ventilation (NIV) or invasive mechanical ventilation (IMV), cardiovascular support includes vasopressor therapy for patients in shock and renal replacement therapy for those with acute kidney injury.

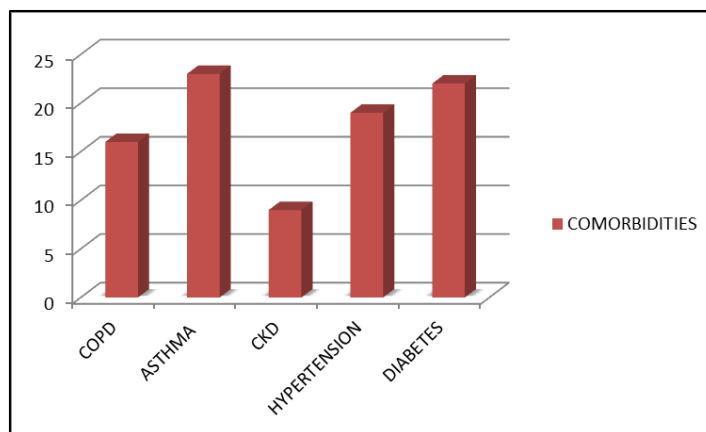
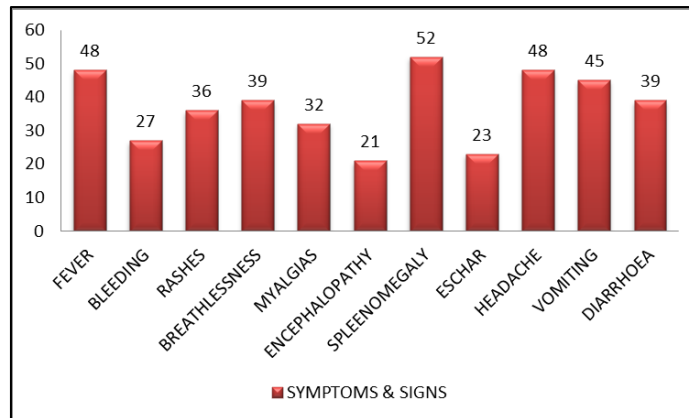
Severity of illness scores (Acute Physiology and Chronic Health Evaluation II, APACHE-II) and Sequential Organ Failure Assessment (SOFA) scores) were calculated at admission. The primary outcome of interest was in-hospital mortality. Secondary outcomes being duration of ICU and hospital stay.

RESULTS

Totally, 71 patients were included in the study who were diagnosed as scrub typhus based on clinical features, positive IgM ELISA and exclusion of other diagnoses.

Table I: Demographic and clinical profile of patients with scrub typhus

Variable	n (%)
Mean	
Total	71
Age	
46.21	
Sex	
Male	38 (53.5)
Female	33 (46.5)
Symptoms & Signs	
Fever	48 (67.6)
Bleeding	27 (38)
Rashes	36 (50.7)
Breathlessness	39 (54.9)
Myalgias	32 (45.1)
Encephalopathy	21 (29.6)
Splenomegaly	52 (73.2)
Eschar	23 (32.4)
Headache	48 (67.6)
Vomiting	45 (63.4)
Diarrhea	39 (54.9)
Comorbidities	
COPD	16 (22.5)
Asthma	23 (32.4)



Baseline patient characteristics were summarized in table I. Of 71 patients, mean age was 46.21 years, 38(53.5%) were male and 33(46.5%) were female. Incidence of symptoms being, fever (67.6%), bleeding (38%), rashes (50.7%), breathlessness (54.9%), myalgias (45%), encephalopathy (29.6%), splenomegaly (73.2%), eschar (32.4%), headache (67.6%), vomiting (63.4%) and diarrhea (54.9%). The admission APACHE-II and SOFA mean scores were 11.57 & 7.83 respectively.

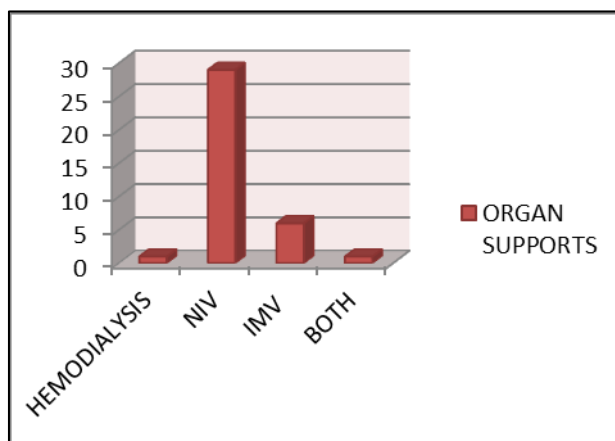
TABLE II : Laboratory investigations

Variable	Mean
Haemoglobin	11.33 gm/dl
Total leucocyte count	13428.87/mm ³
Platelet count	1.89 lakh/mm ³
Serum Creatine	0.86 mg/dl
Serum Sodium	132.54 meq/l
Serum Bicarbonate	22.54 meq/l
Serum Lactate	1.49 mmol/l
Total Bilirubin	1.57 mg/dl
INR	1.50
PTT	20.26 sec
SGOT	180.3 IU
SGPT	140.2 IU

Laboratory analysis was summarized in table II. It showed a mean values of total leucocyte count of 13428.87 cells/mm³, Platelets – 1.89 lakh/mm³, serum creatinine – 0.86 mg/dl, serum sodium-132.54 meq/l, lactate-1.49 mmol/l, total Bilirubin – 1.57 mg/dl, INR-1.50, PTT-20.26 sec, SGOT & SGPT were 180.3 IU and 140.2 IU respectively.

Table III. Interventions and outcome

Variable	n(%)	Mean(number of days)
Vasopressor requirement		
Dopamine	5 (7)	
Noradrenaline	9 (12.7)	
Vasopressin	2 (2.8)	
Transfusion requirements		
Packed cells	1 (1.4)	
Platelets	12 (16.9)	
Other supports		
Haemodialysis	1 (1.4)	
NIV	29 (40.8)	
IMV	6 (8.5)	
Both	1 (1.4)	
Outcome		
Primary		
Mortality	1 (1.4)	
Secondary		
LOS in ICU		4.56
LOS in Hospital		6.98



Data on interventions and outcome during hospitalization was summarized in table III . Of total patients,the vasopressor requirements being Dopamine(7%) , Nor adrenaline(12.7%) & Vasopressin(2.8%).1.4% received packed red blood cell transfusions whereas 16.9% had platelet transfusions . 40.8% required non invasive ventilation whereas 8.5%

required invasive mechanical ventilation and 1.4% required both non invasive and invasive mechanical ventilation . 1.4% of patients required haemodialysis.

The mean duration of ICU and hospital stay were 4.56 and 6.98 days respectively. In hospital mortality was 1.4%.

DISCUSSION

Sinha *et al.* in a prospective study observed the incidence ranging from 3 years to 78 years of age of which 66.66% were females and 33.33% males (Sinha,

P.2014) Madi *et al.* in a retrospective case study reported the incidence to be 70% in females and 30% in males(8). In our study the mean age was 46.21 years

and incidence was found to be 38 (53.53%) male and 33(46.47%) females.

Fever is the most common and first symptom to manifest as observed by Takhar *et al.* (2017). Vivekanandan *et al.* in a prospective study observed that Eschar was seen in 46% and the common sites were axilla, breast and groin (Vivekanandan, M. *et al.*, 2010) in our study the incidence of eschar is found to be 32.4%.

Vivekanandan *et al.* in a prospective observational study of 50 scrub typhus positive cases reported the incidence to be eschar in 46% cases, positive weil felix test in 78% cases, elevation of liver enzymes in 95% of the cases, raised total leucocyte count in 30%, thrombocytopenia in 10% and raised creatinine in 13% cases (Vivekanandan, M. *et al.*, 2010).

Rajoor *et al.* prospectively studied 50 scrub typhus cases and reported the incidence to be, fever in 54% of the cases, raised total leucocyte count in 42% cases, thrombocytopenia in 40% cases, raised creatinine in 14% cases, transaminitis in 86.67% patients, presence of eschar in 12% of cases and positive weil felix test in 94% cases (Rajoor, U. G. *et al.*, 2013).

In a prospective observational study conducted by Mathai *et al.*, on 28 scrub typhus cases found that high leukocyte count was seen in 54% of patients, thrombocytopenia in 43%, deranged transaminase level 88%, abnormal bilirubin level 29% and raised creatinine (37%) (Mathai, E. *et al.*, 2003).

Kim DM *et al.* conducted a prospective case control study on 208 patients to identify the factors associated to severe complications and reported that platelet counts of <100,000/cmm in only 31.5% of patients with severe scrub typhus infection and in 21% in non-severe scrub typhus infection (Kim, D. M. *et al.*, 2010).

In our study we had obtained mean value of total leucocyte count - 13428.87cells/mm³, Platelets – 1.89 lakh/mm³, serum creatinine – 0.86mg/dl, serum sodium-132.54meq/l, lactate-1.49mmol/l, total Bilirubin – 1.57mg/dl, INR-1.50, PTT-20.26sec, SGOT and SGPT were 180.3 IU and 140.2 IU respectively.

In a retrospective study conducted by Mathew Griffith JV *et al.*, on 116 patients to describe the predictors of mortality in scrub typhus patients analysed that the admission APACHE-II scores were significantly higher ($P = 0.007$) in those who needed invasive mechanical ventilation (21.32 ± 8.6) when compared with those requiring non invasive ventilation (16.63 ± 7.24). Actual mortality was lower than predicted APACHE 2 mortality (Mathew Griffith, J. V.

P. et al., 2014). We had found out the mean APACHE – II score to be 11.57 in the present study.

Viswanathan *et al.* has retrospectively analyzed the data from a center in south India and reported the incidence of meningitis in Scrub typhus to be 26.1%. In our study, we found the incidence of encephalopathy to be 21%. (Song, S. W. *et al.*, 2004) Chrispal *et al.* has prospectively reported the odds risk of dying with ARDS to be 3.6 (Chrispal, A. *et al.*, 2010). Song *et al.* has retrospectively reported the incidence of interstitial pneumonia to be 20.8% (Song, S. W. *et al.*, 2004). In our study we had found the incidence of ARDS requiring NIV to be 40.8%, invasive mechanical ventilation to be 8.5% and patients requiring both to be 1.4%.

Kim *et al.* has prospectively reported in a case control study, the incidence of shock requiring vasopressor support to be 7.2% (Kim, D. M. *et al.*, 2010). In our study the incidence of vasopressor requirement being 22.5%.

Griffith *et al.* has retrospectively reported the incidence of haemodialysis in Scrub typhus to be 61.5%. In our study the incidence is found out to be 1.4% (Mathew Griffith, J. V. P. *et al.*, 2014).

Mahajan *et al.* has prospectively reported the mortality to be 14.2% (Mahajan, S. K. *et al.*, 2004). In another prospective study, Kumar *et al.* has reported the mortality to be 17.2% (Kumar, K. *et al.*, 2004). In our study the incidence of mortality is found out to be 1.4%.

CONCLUSION

In our study we hereby conclude that the incidence of organ dysfunction is highly variable compared with other studies whereas the in hospital mortality was relatively low.

REFERENCES

1. Vivekanandan, M., Mani, A., Priya, Y. S., Singh, A. P., Jayakumar, S., & Purty, S. (2010). Outbreak of scrub typhus in Pondicherry. *J Assoc Physicians India*, 58(1), 24-8.
2. Kweon, S. S., Choi, J. S., Lim, H. S., Kim, J. R., Kim, K. Y., Ryu, S. Y., ... & Park, O. (2009). Rapid increase of scrub typhus, South Korea, 2001–2006. *Emerging infectious diseases*, 15(7), 1127.
3. Kim, D. M., Kim, S. W., Choi, S. H., & Yun, N. R. (2010). Clinical and laboratory findings associated with severe scrub typhus. *BMC infectious diseases*, 10(1), 108.
4. Chrispal, A., Boorugu, H., Gopinath, K. G., Prakash, J. A. J., Chandy, S., Abraham, O. C., ... & Thomas, K. (2010). Scrub typhus: an unrecognized threat in South India—clinical profile and predictors of mortality. *Tropical Doctor*, 40(3), 129-133.

5. Rathi, N. B., Rathi, A. N., Goodman, M. H., & Aghai, Z. H. (2011). Rickettsial diseases in central India: proposed clinical scoring system for early detection of spotted fever. *Indian pediatrics*, 48(11), 867-872.
6. Sankhyan, N., Saptharishi, L. G., Sasidaran, K., Kanga, A., & Singhi, S. C. (2014). Clinical profile of scrub typhus in children and its association with hemophagocytic lymphohistiocytosis. *Indian pediatrics*, 51(8), 651-653.
7. Sinha, P., Gupta, S., Dawra, R., & Rijhawan, P. (2014). Recent outbreak of scrub typhus in North Western part of India. *Indian journal of medical microbiology*, 32(3), 247.
8. Madi, D., Achappa, B., Chakrapani, M., Pavan, M. R., Narayanan, S., Yadlapati, S., ... & Mahalingam, S. (2014). Scrub typhus, a reemerging zoonosis—An Indian case series. *Asian Journal of Medical Sciences*, 5(3), 108-111.
9. Takhar, R. P., Bunkar, M. L., Arya, S., Mirdha, N., & Mohd, A. (2017). Scrub typhus: A prospective, observational study during an outbreak in Rajasthan, India. *The National medical journal of India*, 30(2), 69.
10. Rajoor, U. G., Gundikeri, S. K., Sindhur, J. C., & Dhananjaya, M. (2013). Scrub typhus in adults in a teaching hospital in north Karnataka, 2011-2012. *Annals of Tropical Medicine and Public Health*, 6(6), 614.
11. Mathai, E., Rolain, J. M., Verghese, G. M., Abraham, O. C., Mathai, D., Mathai, M., & Raoult, D. (2003). Outbreak of scrub typhus in southern India during the cooler months. *Annals of the New York Academy of Sciences*, 990(1), 359-364.
12. Mathew Griffith, J. V. P., Karthik, G., Ramakrishna, K., Prakash, J. A. J., Kalki, R. C., Varghese, G. M., ... & Abraham, O. C. (2014). Profile of organ dysfunction and predictors of mortality in severe scrub typhus infection requiring intensive care admission. *Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine*, 18(8), 497.
13. Song, S. W., Kim, K. T., Ku, Y. M., Park, S. H., Kim, Y. S., Lee, D. G., ... & Kim, Y. O. (2004). Clinical role of interstitial pneumonia in patients with scrub typhus: a possible marker of disease severity. *Journal of Korean medical science*, 19(5), 668-673.
14. Mahajan, S. K., Rolain, J. M., Kashyap, R., Bakshi, D., Sharma, V., Prasher, B. S., ... & Raoult, D. (2006). Scrub typhus in Himalayas. *Emerging infectious diseases*, 12(10), 1590.
15. Kumar, K., Saxena, V. K., Thomas, T. G., & Lal, S. (2004). Outbreak investigation of scrub typhus in Himachal Pradesh (India). *The Journal of communicable diseases*, 36(4), 277-283.