Spectrum of cardiac manifestations and its relationship to outcomes in patients admitted with scrub typhus infection

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ABSTRACT

Background: Cardiac manifestations in scrub typhus are not well characterized. We describe the spectrum of cardiac manifestations in scrub typhus infection and assess its relationship to outcomes.

Materials and methods: Demographic data, electrocardiographic (ECG) changes, left ventricular (LV) and right ventricular (RV) systolic function, LV diastolic function, myocardial injury (defined as Troponin-T >14 pg/ml) and pericardial effusion were documented. Myocarditis was diagnosed when myocardial injury was associated with global LV systolic dysfunction. Logistic regression analysis was done to assess the impact of myocarditis on ventilatory requirements, length of hospital stay and mortality and expressed as odds ratio (OR) with 95% confidence interval (CI).

Results: The cohort (n= 81; 35 male) aged 49.4±16.1 years (mean ± SD) presented 8.1±3.1 days after symptom onset. The APACHE-II score was 15.7±7.0. Forty-eight patients (59%) were ventilated and 46 (56%) required vasoactive agents; overall mortality was 9.9%. ECG changes were non-specific; sinus tachycardia was the most common finding. Myocardial injury was evident in 61.7% and LV systolic dysfunction in 30.9%. A diagnosis of myocarditis was made in 21% (n=17). Mild diastolic dysfunction was observed in 18%. Mild to moderate pericardial effusion was seen in 51%. Patients with myocarditis had increased ventilatory requirement (OR 4.24, 95%CI 1.11-16.22) and prolonged hospitalization (OR 1.14, 95%CI 1.02-1.27). Myocarditis was not associated with mortality.

Conclusion: In scrub typhus infection cardiac manifestations are frequent and associated with increased morbidity but not mortality.

BACKGROUND

- Scrub typhus, a Rickettsial illness caused by Orientia tsutsugamushi is endemic in the "tsutsugamushi triangle".
- It accounts for nearly 50% of cases of acute undifferentiated febrile illness in some settings (1) and is associated with significant morbidity. -
- The overall case fatality rate of patients admitted to hospital with scrub typhus infection is 9% (2), in those admitted with severe illness to the intensive care unit (ICU), mortality may be as high as 24 % (3).
- It is known that scrub typhus can cause myocarditis and myocardial dysfunction, however the magnitude of this problem and its impact on outcome is unclear.

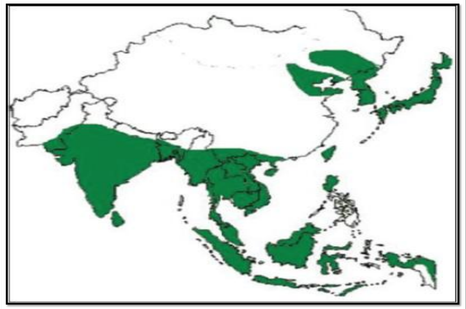
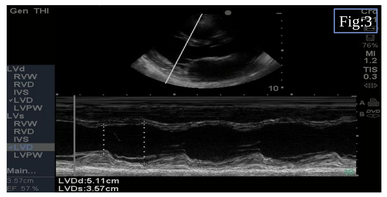


Figure 1:The ‘tsutsughamushi triangle’

MATERIALS AND METHODS

- Adult patients admitted with an acute febrile illness (AFI) during a 20-month period (June 2012 to January 2014) to the medical ward, ICU or high dependency unit (HDU) of a tertiary care teaching hospital in India were included.
- A diagnosis of scrub typhus was made when a patient with an AFI had an eschar (Figure 2) and/or a positive IgM ELISA for scrub typhus and other causes of fever excluded .

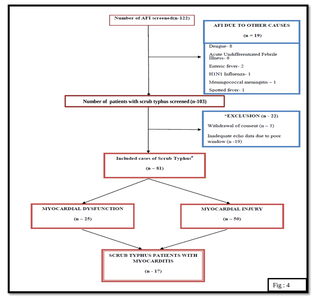
- All patients underwent routine tests that included complete blood count, liver function test, renal function test, electrolytes, chest radiograph and appropriate cultures and serology.
- Cardiac enzymes, creatinine kinase muscle brain isoenzyme (CK-MB) and Troponin-T were determined for all patients.
- A transthoracic echocardiography was performed within 48-hour of admission, using a Sonosite Micromax unit with a 1 to 5 MHz phased array transducer probe.
- LV systolic function was assessed by the ejection fraction (EF), cardiac index (CI), and stroke volume index (SVI).
- LVEF of <50% determined by M mode in the para-sternal long axis view (Figure 3) was considered as myocardial dysfunction.



- A diagnosis of myocarditis was made when global LV systolic dysfunction, with an LVEF of <50%, was associated with cardiac enzyme elevation (Troponin T >14 pg/ml).

RESULTS

- During the study period 122 patients with suspected scrub typhus were screened for myocarditis.
- 103 patients were diagnosed as scrub typhus based on presentation as AFI, a positive IgM ELISA to scrub typhus or a classical eschar and exclusion of other diagnosis(Figure 4).



BASELINE CHARACTERISTICS

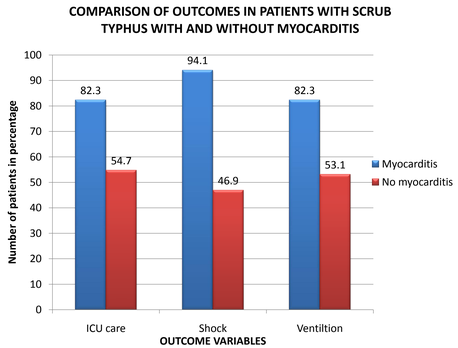
Characteristics	Value
Demographic	
Age, years #	49.41 ± 16.07
Gender ratio (female/male)	46:35
Duration of illness (days) #	8.11 ± 3.11
Symptoms (n)	
Fever	81 (100)
Cough	29 (35.8)
Breathlessness	52 (76.5)
Altered mental status	15 (18.5)
Myalgia	30 (37)
Vomiting	22 (27.2)
Laboratory parameters #	
Hemoglobin, gm %	11.45±2.56
Total counts, cmm	10400±4825.11
Platelets, cmm	69700±70372.34
Serum albumin, gm %	2.58±0.58
SGOT, U/L	139.05±92.39
SGPT, U/L	68.65±49.32
Alkaline phosphatase, U/L	199.14±107.01

(n) Indicates number of patients; values in parenthesis indicate percentage unless specified; # mean, standard deviation; SGOT-serum glutamic-oxaloacetic transaminase; SGPT- serum glutamic pyruvic transaminase

OUTCOME VARIABLES IN PATIENTS WITH SCRUB TYPHUS (n-81)

Primary outcome

Variable	Frequency (%)
Myocarditis	17 (21)
Myocardial dysfunction	25 (30.9)
Myocardial injury	50 (61.7)
Diastolic dysfunction	18 (22.2)



ELECTROCARDIOGRAPHIC FINDINGS IN SCRUB TYPHUS

Sinus Tachycardia	38(46.9)
ST-T changes	10 (12.3)
T wave inversion	8 (9.9)
QRS morphology changes	11 (13.6)
Supraventricular tachycardia	1 (1.2)
Atrial fibrillation	3 (3.7)
Wide QRS tachycardia	1 (1.2)
Sinus bradyarrhythmia	5 (6.2)

UNIVARIATE LOGISTIC REGRESSION OF PREDICTORS OF MYOCARDITIS

Variable	Odds ratio	P value	95% CI
Dialysis	1.875	0.617	0.159 – 22.01
Ventilation	4.242	0.035	1.109 – 16.22
ICU duration	1.212	0.055	0.998 – 1.261
Hospital duration	1.142	0.020	1.021 – 1.278
Hospital outcome	0.509	0.541	0.058 – 4.446

MULTIVARIATE ANALYSIS OF PREDICTORS OF MYOCARDITIS

Variable	0dds ratio	P value	95% C I
Duration of illness	0.7157	0.020	0.5404 – 0.9478
SOFA	1.1348	0.267	0.9078 – 1.418
Duration of hospital stay	1.152	0.059	0.9947 – 1.3345
Ventilation	1.405	0.709	0.2355 – 8.3851

CONCLUSIONS

- In scrub typhus infection cardiac manifestations are frequent and associated with increased morbidity but not mortality.
- The development of myocarditis increased the need for ventilation, prolonged the duration of hospital stay.
- There was no significant clinical, biochemical, hematological or physiological parameters predicting myocarditis, however patients with myocarditis tended to present earlier to the hospital.
- Future histo-pathological studies will help in understanding the patho-physiology.

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