



ORIGINAL RESEARCH PAPER

General Medicine

ECHOLOGICAL ABNORMALITIES IN SEVERE SCRUB TYPHUS PATIENTS

KEY WORDS: Severe scrub typhus, Echocardiographic changes, Severity

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ABSTRACT

Background: Jhalawar is an endemic area for scrub typhus. Scrub typhus presents as an acute, febrile, exanthematous illness. If not treated early, it can lead to life threatening complications, affecting various systems of the body. Hence, this study was done with an objective to study the cardiovascular abnormalities in patients of severe scrub typhus. **Methods:** We conducted a hospital-based study in the Department of Medicine, of a tertiary care hospital in Jhalawar medical college in patients of severe scrub typhus from July 2021 to November 2021. **Results:** Echocardiographic changes included tricuspid regurgitation in 8(16.66%), pericardial effusion in 5(10.41%), myocarditis in 11(22.91%) and Regional wall motion abnormality in 4(8.33%). Left ventricular ejection fraction >45% in 38 (79.16%) and <45% in 10(20.83%). **Conclusions:** Severe scrub typhus manifested with tricuspid regurgitation, myocarditis, pericardial effusion and Regional wall motion abnormality.

INTRODUCTION

Scrub typhus, an acute febrile illness of variable severity is caused by *Orientia tsutsugamushi*. An arthropod vector of the Trombiculidae family transmits it to humans.(1)

This infection is grossly underdiagnosed in India because of its non-specific clinical presentation, low index of suspicion among clinicians, limited awareness about the disease and lack of diagnostic facilities.(2)

Scrub typhus can be cured with antibiotics, if the clinical disease course is not severe, although a delayed diagnosis may lead to severe complications such as pneumonia, acute kidney injury, meningitis, encephalitis, upper gastrointestinal bleeding, and multiple organ failure, as well as the possibility of myocardial infarction or stroke, and some patients may die from such complications.(3)

The skin site of inoculation of *Orientia tsutsugamushi* becomes necrotic and evolves into a painless lesion called eschar. The endothelial cells of vascular lining of various organs are the site of proliferation of *Orientia*. The bacteria attack brain, pancreas, lung, kidney and skin releasing inflammatory mediators like cytokines, prostaglandins, and leukotrienes.(4)

The clinical clues of *Tsutsugamushi* Disease are high fever, rash and eschar formation. The clinical manifestation develops from generalized vasculitis and disseminated intravascular coagulation (5).

The pathologic changes are endothelial oedema, perivasculitis and lymphocytic and monocytic infiltration (6).

Cardiomegaly results from myocarditis, a rare complication with life threatening consequences, but more frequently it results from pericarditis. The mechanism of pericarditis has been explained as a type of systemic vasculitis (5),

Myocarditis is postulated to occur as a result of disseminated endothelial infection of the small vessels or secondary

immune mediated mononuclear inflammation[7].

OBJECTIVES

The primary objectives were to study the spectrum of cardiac manifestations in scrub typhus infection and to estimate the incidence of tricuspid regurgitation, myocarditis, pericardial effusion and Regional wall motion abnormality. This would help understand the disease process better and enable more focused research and treatment.

METHODS

It is a prospective study among 48 patients with scrub typhus who were hospitalized at SRG, Jhalawar medical medical college and Hospital during the period from July 2021 to November 2021.

The patients with scrub typhus were defined as those admitted to the hospital with characteristic eschar and typical clinical symptoms such as fever, chills, headache, and skin rash. Scrub typhus patients also exhibited > 4-fold increases in antibody titers on indirect immunofluorescent antibody tests during the recovery period or received positive diagnoses via nested polymerase chain reaction tests using material obtained from buffy coats or eschar samples.

The patients' age, gender, and underlying health factors, including cigarette smoking, hypertension (HTN), diabetes mellitus (DM), cardiovascular disease, pulmonary disease, hepatic disease, and malignancy were investigated.

A relevant history was recorded. 12 lead ECG was used to record: Heart Rate, Axis, Rhythm, ST changes, T wave changes, Arrhythmias, Bundle Branch Blocks and Ischemia. Echocardiography: Was done using i33 ECHO machine with 2-5 Broadband phase Array probe of Philips Medical System to record-IV volumes, LV mass, Global LV Systolic function, RWMA, I.V.C diameter.

Inclusion Criteria

Patients features consistent with scrub typhus, showing IgM antibodies by ELISA

Age >18 years.

Exclusion Criteria

Patients who died within 12 hours of hospitalization.
 Patients with a history of any cardiac disease.

All patients with features consistent with scrub typhus showing IgM antibodies by ELISA were included in study. The relevant history was recorded in a performa. The hematological and biochemical investigations were performed at the time of admission to hospital. A 12 lead ECG was done and Echocardiography was performed using i33 ECHO machine with 2-5 Broadband phase Array probe of Philips Medical System. Echocardiography was repeated 3 months after discharge from hospital. Left Ventricular Systolic dysfunction was defined as LV Ejection Fraction(LVEF) 45-54% was defined as Mild LV systolic dysfunction, 30-44% as Moderate LV systolic dysfunction and LVEF <30% as Severe LV systolic dysfunction. Left Ventricular Mass/ BSA of 116-131 (g/m)2 in males and 96-108 (g/m)2 in females was defined as Left Ventricular Hypertrophy.9 The data was entered on Microsoft Excel spreadsheet and descriptive analysis for baseline characteristics of patients. Cross tabulation with outcome variable of interest was done using statistical SPSS software version 22.0.0.0 and Epi Info 7.1.5 for windows.

RESULTS

Of the total 48 patients 40 (83.33%) were aged <60 years. 30 (60.50%) were males and 18(37.5%) were females.

On examination of cardiovascular system, 38 (79.16%) patients had tachycardia at time of examination, 12(33.33%) had other added sound i.e. short systolic murmur at apex (Grade II/VI) in 1(2.08%) and pan systolic murmur in tricuspid area in 8(16.66%) patients.

On 2D ECHO, 8(16.66%) had evidence of myocarditis 11(22.91%), tricuspid regurgitation (TR) 8(16.66%), 5(10.41%) had pericardial effusion, RWMA was noted in 4(8.33%) patients. LVEF (Left ventricular ejection fraction) was >45% in 38(79.16%) patients and the remaining 10(20.83%) had EF <45%. Main cardiovascular abnormalities noted in the study group are given in Table no. 1.

Table no. 1 Main Cardiovascular Abnormalities In study group (n=48).

ECHOLOGICAL FINDINGS	NO. OF PATIENTS
LVEF (<45%)	10 (20.38%)
LVEF (>45%)	38 (79.16%)
Tricuspid Regurgitation	8 (16.66%)
Pericardial Effusion	5 (10.41%)
Myocarditis	11 (22.91%)
RWMA	4 (8.33%)

On repeat 2D ECHO after 3 months, pericardial effusion disappeared in all 5 patients. Of total 8 patients with TR, in 7 patients TR disappeared, while there was evidence of mild TR in 1 patient, out of total 4 patients with RWMA 2 was recovered and there was evidence of RWMA in rest 2, out of 11 myocarditis patients 9 was recovered and remaining 2 patients were lost to follow up.

All patients received anti-rickettsial antibiotics in the form of doxycycline, and/or azithromycin (IV, oral). 44(91.66%) patients had hypotension, of which 38(79.16%) were treated with IV fluids and the remaining 6(12.50%) inotropic agents were also used. Of total 44 patients with hypotension, 42(87.50%) improved after treatment. 2 (4.16%) of these 6 patients, who died, had hypotension unresponsive to inotropes.

DISCUSSION

In our study age of study participants ranged from 18 to 80

years. 32(66.66%) patients in our study were in aged <40 years and 16 (33.33%) patients were in age >40 years (40-80 years). The higher incidence in younger and active age group with Male preponderance (62.50%) in the study group has previously been reported.

The various clinical features present in the study group corroborate with most other studies. The presence of eschar was less frequent in our study as compared to other studies. This may be due to the reason that eschar is seen less frequently in the Indian population.

14%. Occurrence of pericarditis on autopsy in 58% patients of scrub typhus. The cardiac complications occurred in 5-25% which included hypotension. (8)

Yotsakura et al reported a case of scrub typhus with myocarditis Rickettsia tsutsugamushi was demonstrated on endomyocardial biopsy.(9)

Chang et al reported pericarditis in a patient of scrub typhus.8 Karthik et al reported mild to moderate pericardial effusion in 51% and myocarditis in 12% patients of scrub typhus.8

Echocardiogram is a key non-invasive tool in detecting impaired IV function in suspected myocarditis, even when subclinical.(10)

Echocardiographic changes in our study included tricuspid regurgitation (TR) in 8(16.66%), RWMA in 4(8.33%) and myocarditis in 11(22.91%). In a study of 48 patients of complicated scrub typhus, myocarditis was found in 11(22.91%).

Nadda et al reported Thirty-two (55%) patients were aged <60 years with female preponderance (72%). Echocardiographic changes included tricuspid regurgitation in 14(24%), pericardial effusion in 4(7%), myocarditis in 1(2%) and Regional wall motion abnormality in 1(2%). Left ventricular ejection fraction >45% in 47 (81%) and <45% in 11(19%). Fifty-one patients had hypotension at presentation and 49 (90%) of them improved. Interestingly, 10 of 11 patients with reduced EF (<45%) survived whereas 6 of total 7 patients, who died, had preserved EF (>45 %).(11)

Marin-Garcia J et al studied Echocardiographic changes in our study included tricuspid regurgitation (TR) with and without pulmonary hypertension (PAH) in 14(24%), RWMA in 1(2%) and myocarditis in 1(2%). In study of 91 patients of complicated scrub typhus, myocarditis was found in 14%. (12)

In our study 44 (91.66%) of the total 48 patients had hypotension at presentation and 42 of them improved and 2 died. In 38 (%) patients, hypotension responded to only intravenous fluids whereas remaining 6 required additional inotropes. All 38 patients who required fluid therapy recovered all but 4 out of 6 patients who required inotropic support recovered and 2 patients died who have LVEF > 45%.

Karthik G et al observed Depressed LVEF in 25 (30.9%) patients. RWMA was seen in 12 patients, of whom seven had a LVEF of < 50%. Although the presence of new RWMA with myocardial injury would suggest myocardial infarction, it is possible that in this clinical setting, it could also indicate focal myocarditis in these seven (8.6%) patients. However, this was not explored further and also observed mild to moderate pericardial effusion in 41 (51%) patients. However, none developed cardiac tamponade requiring intervention.(13)

Ashok kumar et al observed Echocardiography detected reduced ejection fraction (EF) in 30 patients (42.8%) with mild reduction (EF 45-54 %) in 20 (28.5%) and moderate reduction (EF 30-44%) in 10 (14.3%). The age showed a significant

difference with EF (p-value 0.003), and the patients with moderate reduction were younger (mean age of 20.7 ± 5.6 years). Pericardial effusion was found in nine patients (12.9%).(14)

Thap LC et al conducted a prospective study on 51 septic shock patients in Thailand, and scrub typhus was documented in 18 (35%) patients. (15)

On screening English Language Literature, no study was available on the relationship of LV Ejection Fraction on Echocardiography and outcome of patients suffering from scrub typhus. However present literature on effects of sepsis caused due to non-scrub typhus diseases suggest that the mortality increased significantly (70-90%) when sepsis was accompanied with cardiovascular dysfunction in comparison to patients of sepsis without cardiovascular impairment (20%).(16,17)

Jardin et al studied 90 patients of septic shock during later phase of septic shock and concluded that the cardiac function and EF abnormalities were fully reversible after 7 to 10 days of the onset of sepsis. (18)

The septic shock was associated with significant myocardial dysfunction despite increased cardiac output and a normal stroke volume. The end-diastolic volume was higher and EF was lower in survivors when compared to non-survivors of septic shock. (19)

These findings are in agreement with our study where 10 patients had EF <45%, all of them survived and 2 of 38 patients with EF >45% died.

In our study a total 8 patients had TR. All 8 patients reported repeat Echocardiography at 3 months and TR disappeared in 7 patients.

CONCLUSION

Severe scrub typhus can manifest with potentially life threatening cardiovascular complications myocarditis, pericardial effusion, RWMA, valvular involvement and shock. The majority of patients with septic shock respond to antibiotics and fluid resuscitation however a few may require additional support of inotropic agents also. The patients of severe scrub typhus with reduced EF on Echocardiography had better outcomes. Myocarditis, pericardial effusion, RWMA, valvular involvement (TR) should be screened Ecologically for cases of Rickettsial stigmata, especially in an endemic area. Early suspicion and proper management are essential to achieve clinical improvement and reduced mortality. This is an observational study of patients that was conducted on a small sample size. By virtue of the single-center study design, the results may not be generalized to other however an interesting relationship of association of EF on Echocardiography and outcome of patients suffering from severe scrub typhus emerged from this study and this study sets the stage for further randomized control trials encompassing a greater sample size to help better elucidate and confirm our findings.

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