

A Case Series Of Scrub Typhus In Obstetrics

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ABSTRACT

Scrub typhus is endemic and re-emerging in eastern and southern Asia. Illness varies from mild and self-limiting to fatal. Only few studies were published about its effect in maternal and neonatal outcome. A retrospective analysis was done in six prenatal and two postnatal women with scrub typhus. Details about clinical presentation, investigations, treatment given, response to treatment and pregnancy outcome were collected. The common symptoms were fever with chills, vomiting, myalgia, headache and abdominal pain. Typical features of eschar and lymphadenopathy were noted in only two cases. Two patients presented with jaundice and altered liver function test. Two patients presented with breathlessness. One patient developed oligohydramnios. Two postnatal women developed scrub typhus following blood transfusion for postpartum haemorrhage. Because of its high prevalence, scrub typhus should be included in fever investigations in endemic areas, even in the absence of eschar. Early diagnosis of cases will help in less severe organ damage and easy recovery with antibiotics. Few evidences state that scrub typhus can spread through blood transfusion. Correlation between blood transfusion and scrub typhus has to be further evaluated.

Keywords: Complications, Pregnancy, Scrub typhus

INTRODUCTION

Scrub typhus caused by *O. Tsutsugamushi* is spread by bite by trombiculid mites. Disease is endemic and re-emerging in eastern and southern Asia, northern Australia, and islands of the western Pacific and Indian Oceans [1].

Illness varies from mild and self-limiting to fatal. After an incubation period of 6–21 days, onset is characterized by fever, headache, myalgia, cough, and gastrointestinal symptoms. Some patients recover spontaneously after a few days. Classically patient presents with a primary papular lesion, which enlarges, undergoes central necrosis, and crusts to form a flat black eschar. This is associated with regional and later generalized lymphadenopathy. Macular rash may appear on the trunk. These signs are seldom seen in indigenous patients. Fewer than 50% of Westerners develop an eschar, and fewer than 40% develop a rash [1]. If untreated, patient may develop meningitis, encephalitis, cranial nerve deficits, interstitial pneumonia, myocarditis and cardiac dysfunction [2]. Sometimes, palpable spleen and liver may also be present. The case-fatality rate for untreated classic cases is 7% but would probably be lower if all mild cases were diagnosed [1]. Patients with untreated disease remain febrile for about two weeks and have a long convalescence of four to six weeks thereafter [3].

There were several studies about scrub typhus in general population. Only few studies were published about its effect in pregnancy, maternal and neonatal outcome.

MATERIALS AND METHODS

A retrospective analysis was done in six pregnant and two postnatal women with scrub typhus from the Department of Obstetrics and Gynaecology, Sri Manakula Vinayagar Medical College Hospital, Puducherry, India, in four months period from December 2013 to March 2014. Records of pregnant and postnatal women diagnosed with scrub typhus were reviewed. Details such as clinical presentation of patient, associated symptoms, general condition and systemic evaluation were noted. Details of investigations like urine analysis, complete blood count, platelet count, smear for malarial parasites, widal test, serology for dengue, scrub typhus,

renal function test, liver function test and coagulation profile were collected. For diagnosing scrub typhus immunochromatography, which is a rapid diagnostic test was employed. The results were recorded as positive, equivocal, or negative for the presence of IgM and total antibodies. Drug details, duration between starting of antibiotic and subsidence of fever were noted. Details about the delivery route, neonatal conditions were collected. Details about ICU care and additional treatment were also collected.

RESULTS

Total number of fever cases with suspicion of scrub typhus screened in SMVMCH in the year 2013 is 659. Out of it, 340 cases turned out to be positive for scrub typhus. Eight cases were scrub typhus positive in antenatal and postnatal patients. Six patients developed scrub typhus in antenatal period and two got scrub typhus in postnatal period [Table/Fig-1].

The common symptoms are fever with chills, vomiting, myalgia, headache and abdominal pain. Typical feature of eschar and lymphadenopathy were noted only in two cases. Two patients had associated symptom of cough. Two patients presented with jaundice and altered liver function test. Two patients presented with breathlessness. One patient developed oligohydramnios. All patients diagnosed with scrub typhus were started on injection Azithromycin 500 mg once daily for five days. All patients responded within two days of antibiotic treatment. One patient entered into preterm labour and baby died due to hyaline membrane disease. Other five cases delivered uneventfully with good maternal and neonatal outcome. Both postnatal women who developed fever on third day of delivery had atonic PPH at delivery for which blood transfusion was given. On evaluation for fever, scrub typhus turned out to be positive in those two women.

DISCUSSION

Scrub typhus in pregnant women presented with non-specific signs and symptoms similar to non-pregnant patients. Common presenting symptoms in our study are fever with chills, vomiting, myalgia, headache and abdominal pain.

Patient No.	1	2	3	4	5	6	7	8
Fever duration	3 Days	5 days	5 days	3 Days	3 Days	15 Days	4 Days	5 Days
Associated symptom	Vomiting, Head ache, Myalgia, Pain abdomen Dark urine ↓ fetal movements	Chest pain, hlessness, Pain abdomen	joint pain	Head ache, Myalgia	Myalgia	Head ache, Cough	Vomiting	Breathlessness Vomiting, Head ache, Myalgia, Pain abdomen
Signs	Eschar Icterus	Tachycardia, tachpnoea, air hunger, Hypoxia, Abdomen distended	Eschar, Lymphadenopathy	Icterus				Tachycardia, tachpnoea,
Additional complications							Atonic PPH 2 units blood transfused	Atonic PPH 6 Units blood components transfused
Gestational age(wk)	30	27	38	41	33	33	38	39
Renal function	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Liver function test results Bilirubin in mg/dL, SGOT in U/L, SGPT in U/L	1.9/56/50	Normal	Normal	1.8/50/58	Normal	Normal	Normal	Normal
Scrub test	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Drug treatment	Azithromycin	Azithro	Azithro	Azithro	Azithro	Azithro	Azithro	Azithro
Interval between drug and recovery	2 days	3 days	2 days	3 days	2 days	2 days	3 days	4 days
Maternal and fetal outcome	Baby died 3 days of life due to RDS	Mother and baby healthy	Mother and baby healthy	Mother and baby healthy	Mother and baby healthy	Mother and baby healthy	Mother and baby healthy	Mother and baby healthy

[Table/Fig-1]: Presentation and outcome of patients of scrub typhus in obstetrics

The clinical manifestations of this disease range from sub-clinical disease to organ failure to fatal disease. Deaths are attributable to late presentation, delayed diagnosis, and drug resistance [4]. Abdominal pain is a common presenting symptom in scrub typhus patients. Aung-Thu et al., [5] in his study showed that abdominal pain may be due to vasculitis of the gastrointestinal tract in scrub typhus infection. Therefore, scrub typhus should be considered in differential diagnosis of fever and abdominal pain in endemic area.

Kanno et al., showed that liver pathology in scrub typhus is consistent with the features of non-specific reactive hepatitis [6]. They proved that cellular immunity may be the basis behind the pathogenesis of the hepatic injury [6].

Lung pathology is due to diffuse alveolar damage with hyaline membrane formation and interstitial pneumonitis with infiltration of inflammatory cells. Immunohistochemical stain showed *O. Tsutsugamushi* antigen depositions in the endothelial cells [7]. Hence, scrub typhus patients should be carefully evaluated for potential progression to Acute respiratory distress syndrome (ARDS) if they initially have respiratory symptoms.

In our study all pregnant women recovered well without sequel. There was one early neonatal death due to RDS following preterm delivery. Other studies also reported that scrub typhus in pregnancy may be associated with increased foetal loss, [8-9] preterm delivery, [8,10] and small for gestational age infants [9]. There have been reports of vertical transmission [10-11] from transplacental infection and transmission in perinatal blood borne infection during labour [11] causing neonatal scrub typhus in mothers with acute febrile illness during pregnancy.

The oldest test in current use is the Weil-Felix OX-K agglutination reaction, which is inexpensive, easy to perform, and results are available overnight; however, it lacks specificity and sensitivity. Indirect immunofluorescence antibody (IFA) assay and indirect immunoperoxidase (IIP) test are the gold standard diagnostic tests for scrub typhus, but they require highly trained personnel and production of antigens may vary among different laboratories, leading to inconsistencies in the interpretation of results [12]. Moreover these tests are costly. We used the rapid immunochromatography test, which has sensitivity and specificity for the detection of IgM

were 96.8% and 93.3% respectively. For the detection of total antibodies, the sensitivity was 97.6%, but the specificity was much lower, at 71.4% [13].

The recommended treatment regimen for scrub typhus is doxycycline 100 mg bd for 7- 15 days [1,14]. Alternatively chloramphenicol 500 mg qid orally for 7-15 days can be used. Another alternative is azithromycin 500 mg orally for three days. Especially in pregnant women, Azithromycin does not cause harm to the developing foetus. Azithromycin penetrates polymorphonuclear leukocytes and macrophages, which are target cells for *O. Tsutsugamushi*. So Azithromycin seems to be the best option in pregnant women with scrub typhus.

In a case series by Kim et al., there were eight pregnant women with scrub typhus. All were treated with a single 500-mg dose of azithromycin. All patients responded well to the treatment and no relapses were reported. Finally pregnancy showed good maternal and fetal outcome [15].

In a case series by Mahajan et al., there were five cases of scrub typhus in pregnancy. Azithromycin was used in four cases. Out of four cases, three survived and one died. The death was attributed to the late presentation of the patients to the hospital with multiple organs involvement. In one case which was treated with ceftriaxone and doxycycline, maternal response was good with the treatment, but pregnancy ended in preterm labour and delivered a growth restricted baby which died immediately after birth [16].

Whether there is a correlation between blood transfusion and scrub typhus has to be further investigated. In our study two postnatal women developed scrub typhus following blood transfusion for PPH. This led us to search in literature for blood transfusion as mode of transmission of infection. Study on mice by Casleton BG et al., [17] showed that *O. Tsutsugamushi* can survive in an infectious form in blood stored as packed RBCs at 4°C or glycerolized and frozen. Current medical diagnosis and treatment also states that apart from vertical transmission, blood transfusion may also transmit the pathogen [14]. Rare occupational transmission via inhalation is documented among laboratory workers [14].

Early diagnosis of these cases resulted in less severe organ damage and easy recovery with antibiotics.

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