Section: Miscellaneous

Original Research Article

SEROPREVALENCE AND MATERNAL AND FETAL OUTCOMES DUE TO SCRUB TYPHUS IN PREGNANCY IN A TERTIARY CARE HOSPITAL, PATNA

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ABSTRACT

Background: Scrub typhus is a mite-borne infectious disease caused by Orientia tsutsugamushi. It is an important unrecognized cause for undifferentiated acute febrile illness in India associated with poor maternal and fetal outcomes.

Materials and Methods: A prospective cross sectional 1 and half year study was conducted from January 2023 to June 2024 at IGIMS, tertiary care superspeciality teaching hospital, Patna. ELISA was used for testing which is a qualitative test for the detection of IgM antibodies to O. tsusugamushi in serum. All pregnant patients diagnosed with scrub typhus irrespective of period of gestation were studied for detailed clinical profile and outcome.

Results: Among the female 10 (6.5%) tested positive for scrub typhus in pregnancy mostly during later stages of pregnancy. There were 2 preterm deliveries, 1 still birth. Out of the 7-term delivery 1 was LBW and 1 was IUGR. Among the 10 patients, hepatic dysfunction was seen in 6 (60%), renal dysfunction in 4 (40%) respiratory failure in 2 (20%) and sepsis in 2 (20%) cases.

Discussion: My study shows seroprevalence of scrub typhus in pregnancy to be 6.5% which is higher than the study done by Kumar R et al, shimla. In this study, the high proportion of presentations in the third trimester is probably because of referral bias. There was two preterm delivery and 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, preterm delivery and small for gestational age infants.

Conclusion: Although rare, scrub typhus should be considered as differential diagnosis of acute undifferentiated fever in pregnant patients. There is need of increasing awareness of scrub typhus in pregnancy among practitioners as early diagnosis and start of appropriate therapy can prevent fetal loss and improve maternal outcome.

Keywords: Seroprevalence, Maternal and Fetal outcomes, Scrub Typhus, pregnancy, Fever.

INTRODUCTION

Scrub typhus (ST) is an acute fever sickness caused by the bacteria Orientia tsutsugamushi and spread by the larvae (chiggers) of Leptotrombidium mites. ST is endemic in the tsutsugamushi triangle, which stretches from southeastern Asia to the Pacific and

has lately been recorded from various parts of the world outside the tsutsugamushi triangle.[1]

The disease presents with a spectrum of clinical manifestations ranging from self-limited to death, with untreated case fatality reaching as high as 30%.[2]

Acute respiratory distress syndrome (ARDS), myocarditis, acute renal damage, meningoencephalitis, and disseminated intravascular coagulation are all consequences of scrub typhus. Most of the complications of scrub typhus are organ-specific.[3]

It is also an important unrecognized cause for undifferentiated acute febrile illness in India with a high case fatality rate and has been found to be associated with poor fetal outcomes among affected pregnant women.[4]

According to reports, ST has been the most prevalent reemerging rickettsia infection in India. However, while most of the ST reporting comes from tertiary care facilities, teaching hospitals, and academic researchers in specified geographical areas, which means that they do not accurately reflect the disease's prevalence, particularly in India's rural areas, and there is still a dearth of comprehensive data on its prevalence in India.[5]

Doxycycline continues to be the standard therapy for scrub typhus in nonpregnant adults; however, being a class D drug according to the U.S. Food and Drug Administration (FDA), it is contraindicated in pregnant women. Azithromycin has been reported to effectively cure scrub typhus in pregnant women and showed favorable pregnancy outcomes.[6,7]

Recent studies on the clinical characteristics of scrub typhus have reported many abnormal laboratory findings.[8] However, there have been a few studies on the markers for the severity of scrub typhus.[9]

It is necessary to determine the predictors that identify markers of severe disease in order to reduce the mortality due to the high incidence of severe manifestations or complications and the delay in treatment. Based on the markers, severe disease-prone patients can be admitted earlier to a hospital or transferred to a well-equipped institution. Close observation and intensive care can prevent complications and severe morbidity or mortality.

MATERIALS AND METHODS

Study design: A prospective observational study.

Study duration: 1 and half year (18months) study was conducted from January 2023 to June 2024.

Study place: IGIMS, Tertiary care superspeciality teaching hospital, Patna.

Methodology: A Commercially available ELISA kit (InBios International, Seattle, USA), was used for testing which is a test for the detection of IgM antibodies to O. tsusugamushi in serum as per the manufacturer's instructions.

Inclusion Criteria

All female patients above the age of 18 were included in the study.

Out of these all pregnant patients diagnosed with scrub typhus irrespective of period of gestation were studied for detailed clinical profile.

The inclusion criteria included any febrile illness of ≥5 days with clinical features of myalgia, arthralgia, headache, and skin rash, with or without eschar at any site with a positive antibody tests (ELISA test).

Exclusion Criteria

1. Male patients
2. Female patients below 18 years of age.
3. Patients who did not follow up.
4. Patients with other acute febrile illnesses such as malaria, dengue fever, chikungunya fever, enteric fever, and urinary tract infection and cases where antibody tests were negative were excluded from this study.

The clinical profile was observed using a detailed history of symptoms, investigations and the treatment outcomes were noted.

Later, all the pregnant patients were followed up for pregnancy outcome and perinatal complications.

Methodology

Demographic profiles and clinical features such as a history of age, period of gestation, fever, rash, eschar, lymphadenopathy, onset of illness, progression, duration of various symptoms, systemic examination, blood investigations, and vital parameters were noted from the medical records retrieved from the hospital management system (HMS). For fetal outcomes miscarriage, preterm labour, Intra uterine growth retardation, Fetal distress and still birth were noted. In case of maternal outcome maternal mortality, severe illness, ICU admission, respiratory, renal, hepatic cardiac complications and any sepsis were considered. The diagnosis was confirmed by performing a Weil-Felix reaction and/or IgM ELISA on serum samples using the scrub typhus detect test.

Case definitions

Scrub Typhus Cases

These are patients with an acute febrile illness with or without an eschar confirmed by a serological test (specific IgM antibody/Weil-Felix reaction), as described above.

Statistical Analysis

Categorical variables were described in the form of numbers and percentages of patients, while continuous variables were described in the terms of means, medians, ranges, and standard deviations (SDs). The significance of the difference in means and odds ratios (ORs) were calculated using an independent sample t-test. Univariate analysis and binary logistic regression were done as required. The significance of the p-value was taken as $p < 0.05$.

RESULTS

Seroprevalence: Serum specimen from total 840 patients of undifferentiated febrile illness were tested, 153 (18%) were found to be suffering from scrub

typhus. 97 (64%) of patients with scrub typhus were female. Total 10 of 153 patients (6.5%) who were diagnosed with scrub typhus were pregnant.

Trimester wise prevalence: Out of total 10 pregnant patients who tested positive for Scrub typhus, 5 (50%) were found to be in their 3rd trimester, 3 (30%) in their second trimester and 2 (20%) happened to be in their 1st trimester. Its was found that later stage of pregnancy were more effected.

Residence: All the patients effected belonged to the rural background supporting its endemicity and source of infection.

Clinical profile: Various factors were taken into consideration while studying the clinical profile of the patient along with the maternal and foetal outcome. The details of which are shown in the tables below.

Maternal and Fetal Outcome- 2 (20%) deliveries were preterm. 1 still birth. Out of the 7 term delivery 1 was LBW and 1 was IUGR.

All the patients belonged to the age group of 19-37 years and period of gestation between 11-36 weeks. The duration of fever of the patients was between 7 to 12 days. Apart from fever, majorly abdominal pain (80%) was among the chief complaints followed by shortness of breath and icterus (30) each. On examination eschar and rash was found in 40% of the cases. Lymphadenopathy was found in most of the patients (80%). Tachycardia in 60% n tachypnoea in 40% cases.

Complications in patients: Among the 10 patients, hepatic dysfunction was seen in 6 (60%), renal dysfunction in 4 (40%) respiratory failure in 2 (20%) and sepsis in 2 (20%) cases.

Table 1: Clinical profile of patients

Clinical profile	Pt.1	Pt.2	Pt. 3	Pt.4	Pt.5
POG	32	28	11	20	12
FEVER DURATION	7	9	8	10	14
ABDOMINAL PAIN	YES	YES	NO	YES	NO
TACHYCARDIA	YES	YES	NO	NO	NO
TACHYPNOEA	YES	YES	NO	NO	NO
HYPOTENSION	YES	NO	NO	NO	NO
ICTERUS	YES	NO	NO	NO	NO
LYMPHADENOPATHY	NO	YES	NO	YES	YES
ESCHAR	NO	NO	NO	YES	YES
RASH	YES	NO	NO	NO	NO
MATERNAL OUTCOME	SURVIVED	SURVIVED	SURVIVED	SURVIVED	SURVIVED
FOETAL OUTCOME	Preterm delivery at 36 weeks due raised SGPT, fetal bradycardia.	FT	FT	FT	FT

Table 2: Clinical profile of patients

Clinical profile	Pt.6	Pt.7	Pt. 8	Pt.9	Pt.10
POG	34	32	32	35	36
FEVER DURATION	12	7	9	9	11
ABDOMINAL PAIN	YES	YES	NO	YES	YES
TACHYCARDIA	YES	YES	NO	YES	YES
TACHYPNOEA	YES	YES	NO	NO	NO
HYPOTENSION	NO	NO	NO	YES	YES
ICTERUS	YES	NO	NO	NO	YES
LYMPHADENOPATHY	YES	YES	YES	YES	YES
ESCHAR	YES	NO	NO	NO	YES
RASH	NO	YES	YES	YES	NO
MATERNAL OUTCOME	SURVIVED	SURVIVED	SURVIVRD	SURVIVED	SURVIVED
FOETAL OUTCOME	PTD, Emergency c/s-35 weeks d/t oligohyramnios	FT	FT	FT	DIED d/t RDS following birth.

Study	Year	Maternal Mortality (%)	ICU Admission(%)	Respiratory Failure(%)	Cardiac Complication(%)
Kim et al.[6]	2006	1.4	12.1	6.3	3.5
Singh et al.[12]	2020	2.6	15.4	8.3	5.1
Lee et al.[13]	2020	1.2	10.3	5.2	2.9
WHO[14]	2020	1-2	10-20	5-10	2-5
CDC[15]	2022	1-21	10-20	5-10	2-5
Yadav B et al.[17]	2023	3.7	14.8	3.7	00
My Study	2024	00	20	20	00

DISCUSSION

Only a few case reports and case series have been reported in the literature till now of pregnancy with scrub typhus.

Seroprevalence: My study shows seroprevalence of scrub typhus in pregnancy to be 6.5% which is higher than the study done by Kumar R et al, Shimla [10]. In this study, the high proportion of presentations in the third trimester is probably because of referral bias.

Residence: All the patients who tested positive were found to have rural residence which very well corelates to their endemicity and source of infection. This study corresponds to the study of Bahadur A et al.[11]

Trimester wise prevalence: Similar to most studies,[12] done there is preponderance of cases in the later stages of pregnancy

Clinical profile: The comparison between clinical profiles of different studies is shown in the table below.

Trimester wise prevalence: Similar to most studies (Kumar et al,[10]) done there is preponderance of cases in the later stages of pregnancy .

Clinical profile: The comparison between clinical profiles of different studies is shown in the table below.

Maternal and foetal outcome: The comparison between various studies is shown in the table below.

My study showed better maternal outcome with no maternal mortality but bad foetal outcome with 1 miscarriage and 1 still birth. Rest 8 (80%) had no further complications later and were healthy.

Treatment outcome: All the patients were treated with Azithromycin once daily for 5 days. In our study, all patients responded to the treatment and all patients had favourable outcomes even with ARDS patient requiring ventilator support. In some case reports, scrub typhus seems to have adverse effects on pregnancy as reviewed by Kim et al.[6]

There are few articles on scrub typhus during pregnancy. McGready et al,[18] reviewed literature ranging from 1992 to 2014 on both scrub and murine typhus cases in pregnancy. Out of total 97 pregnancies, 15.5% cases (15/97), the outcome was unknown. Remaining 82 cases were studied. Maternal mortality was seen in 2 cases (2.5%). One of the women died before 24 hours of admission while the other died after three days. 17.4% (14/81 cases) had miscarriage and 42% (28/67 cases) reported poor neonatal outcomes (still birth, low birth weight, and preterm labour).

Sengupta et al,[19] in their case series of 42 cases of scrub typhus complicating pregnancy showed thapregnancy loss with scrub typhus was significantly higher as compared to their routine obstetric data: 14 cases (33%) vs 2.8%; P < 0.001.

Table 1: Maternal outcome of patients

Table 2: Foetal outcomes

Study	Year	Miscarriage (%)	Preterm (%)	IUGR (%)	Still Birth (%)
Kim et al.[6]	2006	12.5	26	11	12.6
Singh et al.[12]	2020	15.4	31	13	4
Lee et al.[13]	2020	10.3	22.4	9.5	2.4
WHO[14]	2020	10-20	20-30	10-20	2-5
CDC[15]	2022	10-20	20-30	10-20	2-5
Yadav B et al.[17]	2023	3.7	44	11	3.7
My study	2024	10	20	10	10

CONCLUSION

Although rare, scrub typhus should be considered as differential diagnosis of acute undifferentiated fever in pregnant patients. There is need of increasing awareness of scrub typhus in pregnancy among practitioners as early diagnosis and start of appropriate therapy can prevent foetal loss and improve maternal outcome. Awareness of this disease among doctors at rural endemic setting is still

rudimentary. Treatment with safer antibiotic, Azithromycin should be included in acute undifferentiated fever cases which is a safer antibiotic compared to Doxycycline.

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