

Detection of *Orientia tsutsugamushi* Infection from Stillbirth Cases: Finding from CHAMPS Study in Bangladesh

Muntasir Alam¹, Afruna Rahman¹, Arpita Shyama Deb¹, M Ishrat Jahan¹, Shafina Jahan¹, Kyu Han Lee², Mohammad Zahid Hossain¹, Shams El Arifeen¹, Mustafizur Rahman¹, Emily S. Gurley²

¹International Centre for Diarrhoeal Diseases Research, Bangladesh (icddr,b), Dhaka, Bangladesh; ²Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Background

Orientia tsutsugamushi is a mite-born obligate intracellular gram-negative bacterium known to cause scrub typhus, a febrile illness endemic in the Asia-Pacific region. The infection is treatable with doxycycline. During pregnancy *O. tsutsugamushi* could lead to

- Stillbirth,
- Prematurity
- Low birth weight

Bangladesh falls within the Tsutsugamushi triangle where scrub typhus is endemic. Information of scrub typhus on pregnancy outcome due to *O. tsutsugamushi* infection is unknown from this region. From Child Health and Mortality Prevention Surveillance (CHAMPS) project data we report three stillbirths from rural Bangladesh where *O. tsutsugamushi* was identified using molecular methods.

Methods

The CHAMPS Project implemented minimally invasive tissue sampling (MITS) technique to collect specimens from post-mortem stillbirths and under-5 deaths. Specimens were tested using histopathology, microbial culture and syndrome based Taqman array card (TAC) platform (Fig. 1). Primers for *O. tsutsugamushi* is included in both blood and CSF TAC cards. The laboratory findings along with maternal clinical history, demographic data and verbal autopsy is shared with a panel of experts (DeCoDe panel) to determine the cause of death.

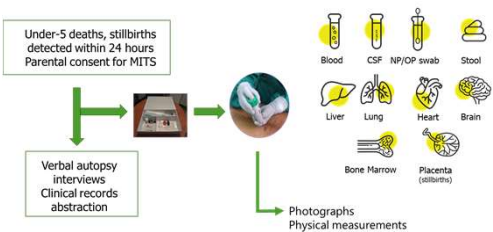
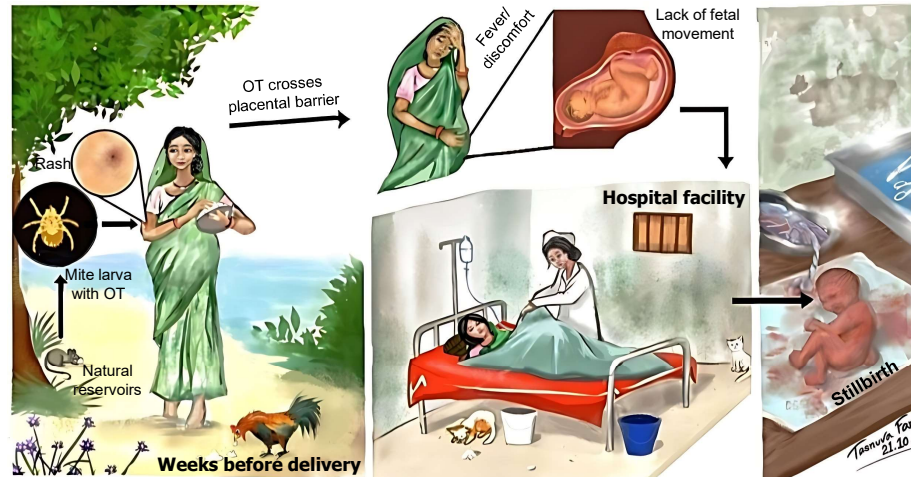


Figure 1. The brief data acquisition protocol for CHAMPS



Pathway of *Orientia tsutsugamushi* mediated stillbirth

Results

O. tsutsugamushi DNA was detected from the postmortem stillbirth specimens

From August 2017 to Aug 2021 specimens from 115 stillbirths were collected. Among the cases, *O. tsutsugamushi* was identified from 3 cases (2%). All three stillbirths were preterm, macerated, low birth weight and detected before delivery by ultrasound or lack of fetal movement (Table -1).

Case No.	Stillbirth type	Gestation age	Body weight	Gross findings	CSF (Ct)	Blood (Ct)
Case 1	Macerated*	35	2445	Sloughing out of skin on Scrotum & abdomen	Pos (34)	Neg
Case 2	Macerated*	35	1965	Hepatomegaly, Nose seepage	Pos (32)	Pos (27-33)
Case 3	Macerated*	34	1946	Hepatomegaly, Nose seepage	Pos (34)	Neg

Table 1: Overall findings of the stillbirth cases. (*) level of maceration was 1 (low =1, extreme = 3)

Maternal complications

Two out of these three cases reported maternal fever days before delivery. One case was prescribed cephradine and metronidazole (Case 1) and another one was (Case 3) prescribed with ciprofloxacin and metronidazole. All of these pregnant women stillbirth were confirmed antepartum (Fig 2).

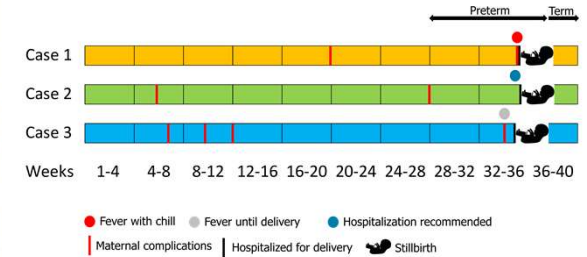


Figure 2. Summary of maternal complications during pregnancy. Maternal complications include feverish, acidity, burning sensation, blurred vision, restlessness, lower abdominal pain etc.

Cause of stillbirths

Intrauterine hypoxia was identified as underlying cause of stillbirth for two cases. For Case 2 Cytomegalovirus (CMV) was identified from Blood, CSF and Lung using TAC resulting in intrauterine CMV infection as cause of stillbirth. *O. tsutsugamushi* was not considered in the causal chain of these stillbirth (Table 2).

Case No.	Underlying CoD	Immediate cause
Case 1	Intrauterine Hypoxia	NA
Case 2	Intrauterine CMV infection	Intrauterine Hypoxia
Case 3	Intrauterine Hypoxia	NA

Table 2: Cause of stillbirths from cases identified with *O. tsutsugamushi*

Conclusions

O. tsutsugamushi was not considered in the causal chain of stillbirth due to lack of maternal laboratory diagnosis, high Ct value in TAC and no previous report on scrub typhus mediated stillbirths in Bangladesh. Ct values were consistent with adult diagnosis cases. Possibility of contamination is unlikely and other acute febrile illness studies identifying *O. tsutsugamushi* in Bangladesh detect high Ct value. Therefore, The real burden and impact of scrub typhus infection among pregnant women in Bangladesh deserves further investigation.