



## ORIENTIA TSUTSUGAMUSHI AND HEPATITIS A COINFECTION IN CHILDREN PRESENTING WITH ACUTE FEBRILE ILLNESS WITH HEPATIC DYSFUNCTION: A CASE SERIES.

<b>Dr. Achinta Mandal</b>	Assistant Professor , Department of Pediatric Medicine, Burdwan Medical College&Hospital, Burdwan, West Bengal.
<b>Dr. Nandita Bhattacharya</b>	Junior Resident, Department of Pediatric Medicine, Burdwan Medical College&Hospital, Burdwan, West Bengal.
<b>Dr. Gargi Mandi</b>	Assistant Professor , Department of Pediatric Medicine, Deben Mahata Government Medical College & Hospital, Purulia, West Bengal.
<b>Dr Sumanta Laha*</b>	Associate Professor, Department of Pediatric Medicine, Burdwan Medical College&Hospital, Burdwan, West Bengal. *Corresponding Author

### ABSTRACT

**Introduction:** Coinfections presenting with overlapping clinical features of two diseases often creates a huge diagnostic challenge in clinical practice. Here we are presenting a case series of pediatric patients of acute hepatitis, admitted in our hospital, who were found to be coinfecting with Hepatitis A virus and Orientia tsutsugamushi. **Method:** Our cases presented with high grade fever, gastrointestinal symptoms like nausea, vomiting, abdominal pain, jaundice, ascites, pedal edema and/or facial puffiness. All the cases had high acute phase reactants like ESR, CRP, deranged liver function tests and anemia. The 2nd patient had ultrasonographic findings suggestive of acute liver injury. Scrub Typhus IgM by ELISA method was positive in all. While searching for other probable causes of acute hepatitis, we found positive serology reports against Hepatitis A virus in all of them. All the children responded well with oral Doxycycline therapy and were discharged in stable condition. **Conclusion:** Children from endemic regions may be coinfecting with Hepatitis A virus and other tropical infection like Orientia tsutsugamushi causing Scrub Typhus.

**KEYWORDS :** Scrub Typhus, Hepatitis A , Jaundice

### INTRODUCTION

Scrub Typhus is a rickettsial disease which is acquired through bites of infected trombiculid mites. It is quite prevalent in Indian subcontinent and is a very important differential diagnosis of any acute febrile illness with multisystem involvement in patients coming from endemic area . Hepatitis A is a well known cause of viral hepatitis more prevalent in areas with poor sanitation and hygiene. Both the infections may present with jaundice and hepatic dysfunction along with fever. Elevated liver transaminases can be present in Scrub Typhus in up to 90% of patients(1). On the other hand, acute Hepatitis A can present with atypical symptoms such as high grade fever, headache, myalgia, rash, cervical lymphadenopathy, arthritis and can result in difficulty in diagnosis. So, when these two diseases coexist, the diagnosis becomes a real challenge for the clinician. Here we have presented a case series of combined Hepatitis A and scrub typhus due to its rarity in published literature.

### MATERIAL & METHOD

**Case 1:** A 3 years 6 months old male child was admitted with complaints of high grade fever for 7 days followed by nausea, vomiting, yellowish discoloration of skin and eyes, passage of dark colored urine for 5 days with pedal edema and abdominal distension for 4 days. On general physical examination he had : icterus, pallor, facial puffiness, pedal edema, maculo-papular rash over lower limbs and abdomen and soft tender hepatomegaly and mild ascites. Significant laboratory findings were anemia, leucopenia, raised ESR and CRP and deranged liver function showing total bilirubin 6.2 mg/dl, ALT 835 IU/L, AST 471 IU/L, serum albumin 2.5 mg/dl. We sent fever profile including Scrub Typhus IgM after discovering an eschar on the nape of his neck. The child was started empirical antibiotics with no improvement. We started oral doxycycline after his serology came out to be positive against Scrub Typhus IgM and negative for dengue, malaria and enteric fever. Child became afebrile within 48 hours but due to persistence of jaundice we sent viral markers of hepatitis where Hepatitis A IgM came to be positive. After 7 days, the child was discharged in stable condition.

**Case 2:** A 8 years old girl presented with high grade intermittent fever for last 7 days, pain abdomen, itching, high colored urine and jaundice for 4 days. On clinical examination, she had icterus, pallor, bilateral cervical lymphadenopathy largest measuring 2 cm, moderate ascites with soft and tender hepatomegaly . There was no rash or eschar. We sent fever profile along with viral markers keeping in mind the diagnosis of viral hepatitis.

Her significant laboratory findings were anaemia, leucocytosis, increased acute phase reactants, rise in both conjugated and unconjugated fraction of bilirubin, hypoalbuminemia and 10 fold rise in liver transaminases. USG abdomen showed slightly raised echotexture of liver parenchyma and her serology came positive for Hepatitis A IgM. The child was receiving supportive and symptomatic treatment but the fever was still persisting without any other cause. Further investigations revealed positive Scrub Typhus IgM antibody. After starting oral Doxycycline child started improving clinically, fever subsided and discharged in stable condition.

**Case 3:** A 6 years old boy admitted with fever for 10 days; headache, vomiting, abdominal pain and jaundice for 7 days. On general physical examination, we found icterus, pallor and mild pedal edema. Per abdominal examination revealed hepatosplenomegaly and ascites. In laboratory reports, anemia, slightly decreased platelet count, raised ESR and CRP, hyperbilirubinemia and increased transaminases were found.

Clinical and laboratory findings guided us to think about infection with any hepatotropic virus. We sent blood investigations for markers of Hepatitis virus infection and anti HAV IgM came out to be positive. The child was already on supportive treatment, but he remained febrile even after 5 days of hospital admission. Meanwhile one eschar mark was discovered over scrotum which raised strong suspicion for Scrub Typhus. Blood investigation was sent and high titer of Scrub Typhus IgM was found. We started oral Doxycycline and the child became afebrile within 48 hours.

**RESULTS****Table 1: Clinico-epidemiological Profile Of Three Cases**

Parameters	Case 1	Case 2	Case 3
Age	3y6m	8y	6y
Sex	Male	Female	Male
Residence	Rural	Rural	Rural
Duration of fever	7days	7days	10days
Abdominal pain, vomiting	+	+	+
High colored urine	+	+	-
Clay colored stool	-	+	-
Itching	-	+	-
Joint pain	-	-	+
Icterus	+	+	+
Maculopapular rash	+	-	-
Edema/ascites	+	+	+
Lymphadenopathy	-	+	-
Hepatomegaly	+	+	+
Eschar	+	-	+

**Table 2: Important Laboratory Parameters Of Three Cases**

Parameters	Case 1	Case 2	Case 3
Hb%(gm/dL)	8.5	8.9	9.5
TLC(per cu mm)	4500	11100	8500
Platelet (per cu mm)	2,44,000	1,80,000	1,30,000
ESR(mm/hr)	55	80	65
CRP(mg/L)	9.4	21	34
Bilirubin(conj+unconj)	6.2(4.7+1.5)	6.8(3.0+3.8)	4.2(2.6+1.6)
SGPT(U/L)	835	1072	675
SGOT(U/L)	471	1274	374
Serum albumin(g/dL)	2.5	2.0	2.4
Anti HAV IgM	5.58(+)	5.79(+)	5.63(+)
Scrub IgM	+	+	+

**DISCUSSION**

Scrub Typhus is a vector borne zoonotic infection caused by the gram negative bacteria *Orientia tsutsugamushi* and transmitted to humans by the bite of larval forms of trombiculide mites. It is among the clinically significant rickettsial infections worldwide and commonest reemerging rickettsial disease prevalent in India(2). Clinical presentation varies from nonspecific febrile illness to multisystemic involvement including meningitis or acute encephalitic syndrome, shock, myocarditis, transient bone marrow suppression, acute kidney injury and hepatic dysfunction. Elevation of liver enzymes is mostly mild to moderate in case of Scrub Typhus. Scrub hepatitis with high liver transaminases (>5 fold elevation) is very rare (3). But in our cases, there was marked rise in liver enzymes. Probably it was due to the combined effect caused by two infections though the mechanisms of liver injury are not the same. Scrub Typhus causes cytopathic injury to Kupffer cells, hepatocytes and sinusoidal endothelial cell vasculitis in contrast to Hepatitis A which mainly causes non cytopathic injury secondary to host immune response (4,5). In rare instances, Scrub Typhus may also cause acute hepatic failure (6). That is why Scrub Typhus must be kept as close differential in any sick child coming from endemic regions presenting with acute undifferentiated fever with hepatic dysfunction.

**CONCLUSION**

This case series shows co-existence of Hepatitis A and Scrub Typhus in same patients. So when a child presented with high fever and viral hepatitis like features, we should have a high index of suspicion for Scrub Typhus even if Hepatitis A IgM came positive. Similarly persistence of jaundice in a scrub IgM positive child should prompt the investigations for viral hepatitis. Early detection of such coinfections may save the lives of many child in future.

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**Conflict Of Interest:** None

**REFERENCES**

1. Hu ML, Liu JW, Wu KL et al. Short report: abnormal liver function in Scrub Typhus. *Am J Trop Med Hyg* 2005;73:667-8.
2. Devasagayam E, Dayanand D, Kundu D, Kamath MS, Kirubakaran R, Varghese GM(2021) The burden of Scrub Typhus in India: A systematic review. *PLoS Negl Trop Dis* 15(7): e0009619.
3. Malhotra Y, Ahmad S, Dhar M, Mittal G, Bhat NK, Shirazi N. Rare Causal Association of Scrub Typhus and Fulminant Hepatic Failure. *Online J Health Allied Scs*. 2015;14(2):7
4. Ching-Huei Y. Role of Scrub Typhus in Hepatic Dysfunction: Focus on Acute Hepatitis in Differentiating it from other Causes. *J Bacterial Parasitol* 3:128
5. Lee J, Min Kim D, Na Ra Yun et al. A Comparative Study of Hepatitis Caused by Scrub Typhus and Viral Hepatitis A in South Korea. *Am J Trop Med Hyg* 2011;85(5): 873-77
6. Deepak NA, Patel ND. Differential diagnosis of acute liver failure in India. *Am Hepatol* 2006;5:150-6