

**CLINICAL AND LABORATORY PROFILE OF ADMITTED PATIENTS PRESENTING WITH FEBRILE ILLNESS DUE TO DENGUE AND SCRUB TYPHUS COINFECTION FROM A TERTIARY CARE HOSPITAL IN SOUTH RAJASTHAN, INDIA****MANISH KULSHRESTHA<sup>1</sup>, MEGHA SHARMA<sup>2</sup>, NEELIMA VARANIA<sup>2</sup>, SUSHANT JOSHI<sup>3</sup>, ANJALI KULSHRESTHA<sup>2\*</sup>**<sup>1</sup>Department of Medicine, Ananta Institute of Medical Sciences and Research Center, Rajsamand, Rajasthan, India, <sup>2</sup>Department of Microbiology, Ananta Institute of Medical Sciences and Research Center, Rajsamand, Rajasthan, India. <sup>3</sup>Department of ENT, Ananta Institute of Medical Sciences and Research Center, Rajsamand, Rajasthan, India.\*Corresponding author: Dr Anjali Kulshrestha; Email: [anjalikulshrestha2185@gmail.com](mailto:anjalikulshrestha2185@gmail.com)

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**ABSTRACT****Objective:** The present study aims at describing the clinical features, laboratory diagnosis, and complications in patients presenting with febrile illness due to scrub typhus and dengue coinfection from Southern Rajasthan, India.**Method:** This present prospective, observational, and hospital-based study conducted in the Department of Microbiology of AIMS & RC, Rajsamand, located in Southern Rajasthan, from January 2021 to December 2021. Scrub typhus was diagnosed in the microbiology laboratory by performing SD Bioline, one-step scrub typhus for the detection of IgM antibody, and dengue fever using J.mitra and Co. Pvt. Ltd., rapid card test for the detection of NS1 antigen and IgM antibody.**Result:** Out of 500 patients suspected of AUFI, 25 (5%) patients diagnosed of having dengue and scrub typhus coinfection. Fever was present in all 25 (100%) patients and 13 (52%) of patients had arthralgia, nausea, and vomiting. The most common sign noticed in our study was pallor and icterus in 10 (40%) patients each followed by shock/hypotension in 8 (32%) and hepatosplenomegaly in 5 (20%). The most predominant laboratory finding was thrombocytopenia ( $<1.0 \times 10^6/\text{cumm}$ ) in 23 (92%) patients, while elevated bilirubin ( $>2 \text{ mg/dl}$ ) in 22 (88%) and elevated transaminase and prolonged aPTT in 21 (84%) patients each. The majority of patients 23 (92%) had hepatic dysfunction, i.e., in followed by multi-organ dysfunction (MODS) in 15 (60%).**Conclusion:** In developing countries like India, particularly in tropical areas, dengue, and scrub typhus coinfection is under-recognized entity. Additional investigation should be carried out in cases of AUFI patients with features such as hypotension, leukocytosis, early drop in platelet counts, and hypoalbuminemia.**Keywords:** AUFI, scrub typhus, dengue, coinfection.© 2024 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2024v17i6.50181>. Journal homepage: <https://innovareacademics.in/journals/index.php/ajpcr>**INTRODUCTION**

Scrub typhus is the second most common rickettsial disease caused by *Orientia tsutsugamushi*, a Gram-negative bacterium [1] causing fatal zoonotic infections spread by the bite of infected chiggers mite belonging to Trombiculidae family. It causes acute undifferentiated febrile illness (AUFI) with multiorgan failure [2]. It is reemerging infections encountered in various parts of India, especially in Southern part of Rajasthan [3].

Dengue is vector-borne disease caused by the four serotypes, DENV 1, 2, 3, and 4 of the dengue virus, belonging to Flaviviridae family [4]. The virus transmitted by the bite of female *Aedes aegypti* mosquitoes. According to the WHO guidelines (updated on 2009), dengue fever classified into probable dengue, dengue with warning signs, and severe dengue. In India, case fatality rates (CFR) of approximately 3%-5% have been reported by the WHO [5].

During monsoon and post-monsoon season, an increase in dengue and scrub typhus coinfection in endemic area may cause difficulty in diagnosis which in turn lead to high morbidity and mortality in these patients. Although the vectors for both infections are different, they have similar clinical and laboratory features such as hepatic dysfunction and thrombocytopenia.

In India, there are very few studies available on dengue and scrub typhus coinfection, and early diagnosis of this will help in better outcome of these patients. Keeping the above points in mind, this study was planned with the aim to know the clinical and laboratory profile of patients with dengue and scrub typhus coinfection which will in turn help physicians to diagnose and manage these patients in a better way.

**THOD**

This present prospective, observational, and hospital-based study was conducted in the Department of Microbiology of AIMS & RC, Rajsamand, located in Southern Rajasthan, from January 2021 to December 2021 and ethical clearance was obtained from the Institutional Ethical Committee.

The patients were enrolled in the study who fulfilled the following inclusion and exclusion criteria –

**Inclusion criteria**

The following criteria were included in the study:

1. Patients who were tested positive for IgM antibodies for *O. tsutsugamushi*.

- Patients who were tested positive for NS1 antigen and IgM antibodies for dengue virus.

#### Exclusion criteria

The following criteria were excluded from the study:

- Patients who presented with other causes of fever such as pneumonia, malaria, Leptospirosis, viral diseases, urinary tract infections, and typhoid fever,
- Patients who were tested negative for IgM antibodies for *O. tsutsugamushi* and NS1 antigen and IgM antibodies for dengue virus.

Demographic data, detailed clinical history, physical examination, and reports of standard set of investigation and complications were obtained from the case file. Scrub typhus was diagnosed in the microbiology laboratory by performing SD Bioline, one-step scrub typhus for the detection of IgM antibody and dengue fever using J.mitra and Co. Pvt. Ltd., rapid card test for detection of NS1 antigen and IgM antibody. Statistical analysis was done by the Graph Pad Prism statistical software.

## RESULTS AND DISCUSSION

During the study period, a total of 500 samples were processed in the Microbiology laboratory received from various clinical departments of Ananta Institute of Medical Sciences and Research Center, Rajsamand. Twenty-five samples were diagnosed to have dengue and scrub typhus coinfection (5%). Twenty-five (100%) patients had high grade, continuous fever, arthralgia, nausea, and vomiting in 13 (52%) patients each, jaundice in 10 (40%), and headache and loss of appetite in 6 (24%) patients each.

The most common clinical sign observed in our study was pallor and icterus in 10 (40%) patients each followed by shock/hypotension, hepatosplenomegaly, and eschar in 8 (32%), 5 (20%), and 1 (4%) patient, respectively. The most predominant laboratory finding was thrombocytopenia ( $<1.0 \times 10^6/\text{cumm}$ ) in 23 (92%) patients, while elevated bilirubin ( $>2 \text{ mg/dl}$ ) in 22 (88%), elevated transaminase and prolonged aPTT in 21 (84%) patients each, increased serum urea/creatinine in 19 (76%), hypoalbuminemia in 17 (68%), leukopenia (4000-11000) in 13 (52%), anemia (hemoglobin  $<10 \text{ gm/dl}$ ) in 10 (40%), and leukocytosis (WBC count  $>11,000/\text{mm}^3$ ) in 7 (28%) patients.

The most common complication observed was hepatic dysfunction in 23 (92%) patients followed by multiorgan dysfunction (MODS), acute renal failure, hypotension, encephalopathy, and acute respiratory distress syndrome (ARDS) in 15 (60%), 12 (48%), 8 (32%), 3 (12%) and 2 (8%) patients, respectively.

Scrub typhus is one of the reemerging, most neglected, potentially fatal zoonotic disease encountered in India [2]. It is also one of the most common causes of acute respiratory distress syndrome requiring hospitalization due to complications such as multiorgan dysfunction due pulmonary, neurological, renal, cardiac, or hepatic manifestations leading to a high case fatality rate [3]. Dengue emerged as a major global public health challenge in the tropic and subtropic nations, especially in India. Dengue virus infection presents with a diverse clinical picture that ranges from asymptomatic illness to DF to the severe illness of dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS). Early and accurate diagnosis is critical to reduce mortality [4,5].

Concurrent infection with different pathogens is common in topical areas of India, especially of dengue and scrub typhus coinfection leading to several diagnostic and management challenges. These cases are clustered during monsoon and post-monsoon season. Various studies are available on coinfection of dengue with leptospirosis, malaria, and *Salmonella typhi*. To the best of my knowledge, very few studies have been documented from India including Southern Rajasthan, for

**Table 1: Clinical profile of patients with dengue and scrub typhus coinfection**

Characteristic	No of cases	%
Symptoms		
Fever	25	100
Nausea/vomiting	13	52
Headache	6	24
Jaundice	10	40
Loss of Appetite	6	24
Arthralgia	13	52
Signs		
Pallor	10	40
Icterus	10	40
Shock/Hypotension	8	32
Hepatomegaly	5	20
Splenomegaly	5	20
Eschar	1	4

**Table 2: Laboratory investigation of patients with dengue and scrub typhus coinfection**

Characteristics	No of cases	%
Total leucocyte count		
<4000	5	20
4000-11000	13	52
>11000	7	28
Hemoglobin ( $<10 \text{ gm/dl}$ )	10	40
Platelet count ( $<1.0 \times 10^6/\text{cumm}$ )	23	92
Elevated transaminase	21	84
Elevated bilirubin ( $>2 \text{ mg/dl}$ )	22	88
Increased serum urea/creatinine	19	76
Hypoalbuminemia	17	68
Prolonged aPTT time	21	84

**Table 3: Complications of patients with dengue and scrub typhus coinfection in our study**

Characteristics	No of cases	%
Hepatic dysfunction	23	92
Renal dysfunction	12	48
Hypotension	4	16
Acute respiratory distress syndrome	2	8
Multiorgan dysfunction syndrome	15	60
Encephalopathy	3	12

that reason, this study was planned to know the clinical laboratory profile and complications of patients with dengue and scrub typhus coinfection [2-5].

In the present study, dengue and scrub typhus coinfection was found in 25 (5%) patients. The study conducted by Pandey *et al.* [6], Raina *et al.* [7], and Mittal *et al.* [8] revealed this observation in 0.15%, 1.3%, and 1.88% of patients, respectively. In compassion with these studies, our study showed a higher rate of coinfection, the reason behind this may be because southern Rajasthan has highlands, hills, waterways, grasslands or plains, lakes, valleys, and flatlands leading to the establishment of zoonotic tetrad thus enhancing the transmission of dengue and scrub typhus infection [3].

In the present study, all 25 patients had a fever (100%) during the course of illness. It is followed by arthralgia and nausea-vomiting in 13 (52%) patients each. These observations are similar to the study conducted by Aneesh Basheer *et al.* [9] and Ahmed *et al.* [10], where they found, fever followed by headache and arthralgia among the most common symptoms. In the present study, pallor and icterus were present in 40% followed by hepatosplenomegaly (20%). Similar findings were observed in the study conducted by Sapkota *et al.* [11],

in which patients with coinfection had pallor compared to those with dengue and scrub typhus alone. A study conducted by Visha Singh *et al.* [12] noted that their patients with coinfection had no pallor, this finding is dissimilar to our study.

In our study, among the laboratory investigations, 92% of patients had thrombocytopenia. Low platelet counts are typically associated with both dengue and scrub typhus infection, but much lower platelet counts are present in coinfection. Severe thrombocytopenia in early disease course should raise the suspicion of dengue and scrub typhus coinfection in endemic areas during monsoon and post-monsoon season. These findings are similar to the study performed by Aneesh Basheer *et al.* [9] and Ahmed *et al.* [10], where they noticed that it takes lesser time to attain lower platelet count in patients with coinfection.

As noted in our study aspartate transaminase and alanine transaminase levels were elevated. These inferences were similar to the study conducted by Kim *et al.* [13] and Iqbal *et al.* [14]. It has been observed in both these seasonal diseases individually that aspartate transaminase is more raised than alanine transaminase, still in coinfection both the transaminases are significantly higher as compared with infection caused by dengue or scrub typhus alone. Hypoalbuminemia and elevated aPTT are observed in 68% and 84% of patients, respectively. These findings may occur due to liver dysfunction and these parameters may be deranged more severely in coinfection.

## CONCLUSION

Either single or many organisms are responsible for the causation of acute undifferentiated febrile illness (AUI). In developing countries such as India, particularly in tropical areas, dengue and scrub typhus coinfection are under-recognized in concurrent infections. Additional microbiological investigation should be carried out in cases of patients with AUI having features such as hypotension, leukocytosis, early drop in platelet counts, and hypoalbuminemia.

Early diagnosis will have a significant impact on patient's clinical conditions which in turn will decrease hospital stay along with cost of its therapy. To the best of our knowledge, it is the first prospective study carried out from Southern Rajasthan describing the clinicolaboratory profile along with complications associated with patients with dengue and scrub typhus coinfection. More and more such extensive prospective studies should be carried out to estimate the exact magnitude and impact of this coinfection.

## AUTHORS CONTRIBUTION

All the authors collected data, reviewed and drafted the manuscript, and also approved the final version of this in the end.

## CONFLICTS OF INTERESTS

None.

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