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DENGUE AND SCRUB TYPHUS COINFECTION PRESENTING AS AN ACUTE FEBRILE ILLNESS

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Running Title: Coinfection of Dengue and Scrub typhus.

Abstract:

In India, many time witness coinfection of Dengue and scrub typhus during monsoon and post monsoon period as an acute febrile illness. The aim and objective of present study is to assess the prevalence of coinfection in our rural hospital in acute febrile cases. we found that 0.15% of patients was having dual infection of dengue and scrub typhus among the patients admitted during last year.

Key words: dengue, scrub typhus, Dengue Ns1Ag, IgM antibody for dengue and scrub

Introduction:

In tropical countries including India Dengue, Scrub typhus, Malaria, Typhoid & Leptospirosis are common causes of acute febrile illness ⁽¹⁾. In acute febrile condition, when a patient complains of fever, additional clinical symptoms needs to be correlated for diagnosis and further treatment. During the seasonal increase in dengue cases, concomitant scrub typhus infection in endemic areas can cause a diagnostic dilemma. Dengue is a common arbovirus infection with worldwide prevalence⁽²⁾. It is transmitted by the bite of vectors Aedes aegypti mosquito. Second important cause of febrile illness is scrub typhus is caused by an obligate intracellular, gram negative bacteria, transmitted by a bite of trombiculid mite, the chigger ⁽³⁾.

Both diseases have several similar clinical and laboratory features including rash, thrombocytopenia, and hepatic dysfunction. However, concurrent infection with both pathogens is exceedingly rare, primarily due to the different vectors involved⁽⁴⁾.

And if it is there, then treatments of these co infections pose a therapeutic challenge to the treating physician because of the difficulty in early diagnosis due to overlapping clinical

features. Here, we have done a retrospective analysis of last one year from January to December 2020 to assess the prevalence of dengue and scrub typhus coinfection among patients of acute febrile illness in our hospital.

Material and methods:

Study was conducted in the department of Microbiology MGIMS, Sewagram. In this, we have done retrospective analysis of samples received and processed from 1st January to 31st December 2020. All these patients were visited our tertiary care hospital with a history of fever. After examination by clinician, patients sample were sent to the Microbiology department for blood investigation. For serological diagnosis of acute febrile illness, as per requisition we looked for dengue both IgM antibody and NS1 Ag, Scrub typhus IgM Antibody, Malarial antigen, IgM antibodies of Leptospira, Chikungunya and Japanese encephalitis and Widal test to rule out enteric fever. Dengue IgM antibody and NS1Ag detection was done by using ELISA of Panbio ELISA kit. Scrub typhus IgM detection by Inbios IgM ELISA kit, rapid card test for Malaria of SD BioLine which test for HRP II antigen of Plasmodium falciparum and pLDH antigen of Plasmodium vivax, leptospira IgM antibody by and Widal by tube agglutination test (SPAN Diagnostic) and Enteroscreen of Zephyr Biomedicals. Blood culture are also done as per requisition in laboratory.

Results:

For the 2020 year, we have received total 45,348 serum samples for serological investigations from January to December 2020. Out of that, 15938 (35.15%) were tested for acute febrile illness. These samples were sent directly to the laboratory for investigation by clinician. Out of 15938, 6860 (43.04%) were tested for dengue both NS1Ag and IgM antibody and 3424 (21.48%) were tested for Scrub typhus IgM antibody. In our laboratory we also look for Leptospira IgM antibody, antibodies for Enteric fever by Widal or Enteroscreen and Malarial antigen.

Both scrub and dengue antibodies detection were done by ELISA. Out of total 6860 tested for dengue, 669 (9.75%) were found to be positive for IgM antibody and 269 (3.92%) were found to be positive for NS1Ag. 105 (1.53%) were positive for both NS1Ag and IgM antibody. Out of 3424, 163 (4.76%) were positive for scrub typhus IgM antibody.

Out of total 10284 tested for both, dengue and scrub typhus by ELISA, both antibodies were detected in 15 (0.15%). All these serum samples were tested negative for dengue NS1Ag. We found that coinfection was more in male (60%) than female (40%). Patients were having fever with chills and myalgia as a common symptom. Other associated symptoms were lymphadenopathy, hepatosplenomegaly, cough, rash, jaundice, abdominal pain, altered sensorium, diarrhea, vomiting is listed in Table 1. Table 2 shows different laboratory parameters in dengue and scrub typhus coinfection patient.

Samples were also tested for other etiology causes acute febrile illness like malaria, enteric fever, Leptospira, chikungunya and Japanese encephalitis as per requisition. Out of 15938, 3344 (20.98%) were tested for malaria, 1145 (7.18%) for Enteroscreen, 350 (2.19%) for widal and 815 (5.11%) for Leptospira . None of the sample was tested for Chikungunya and Japanese encephalitis as they were not raised for investigation by clinicians.

We found that 3 (0.09%) were positive for Malarial antigen (Pl. falciparum HRP-II), 22 (1.92%) samples were positive for S.Typhi IgM antibody by Enteroscreen, widal was positive only in 1 (0.28%) patient. None of the sample was found to be positive for Leptospira IgM antibody.

Discussion:

People residing in tropical countries like India, suffer from acute undifferentiated fevers during monsoons and post-monsoons periods. In many parts of India, dengue and scrub typhus infections together comprise more than half of all acute undifferentiated febrile illnesses⁽⁵⁾. We also found that in_acute undifferentiated fever cases, dengue and scrub typhus infections are more than any other infection. Among them coinfections are also reported. This may be due to tropical Indian climate provides an environment conducive for the propagation and transmission of both these infections.

In our hospital, we found dual infection of dengue and scrub typhus with prevalence rate was 0.15%. Similar findings were noted by Raina et al was 1.3% (6), in Uttarakhand by Mittal et al was 1.88% (7). also reported from tertiary care hospital in southern coast of India (8). Due to growing population, frequent travels, better laboratory services and more awareness, coinfection are emerging as a major concern in tropical countries. Dual infection concurrently results in illness with overlapping symptoms. It further makes the diagnosis and management of such patients challenging.

These might be true mixed infections and not due to serological cross reactivity. The aetiologic agents responsible for this infectious disease are members of different families. Scrub typhus is caused by *Orientia tsutsugamushi*, a Gram negative bacilli and dengue is due to single stranded RNA virus belonging to Flavivirus group.

Mixed infections are of concern for a clinician including unexpected clinical findings and apparent poor response to treatment. Role of coinfections in the severity of the disease is not clearly identified⁽⁹⁾

Delay in diagnosis and initiation of appropriate antibiotic therapy can be associated with mortality in 14%–20% of patients (10,11,12,13). Hence, early recognition and prompt antibiotic therapy is crucial in the management of acute undifferentiated fever. Dengue is a mosquitoborne infection caused by one of the four dengue virus serotypes that belong to the genus Flavivirus. Despite supportive management, mortality rate due to dengue hemorrhagic fever and dengue shock syndrome (DSS) ranges from 3% to 11% among adults (14,15). Early diagnosis can improve patient outcomes and promote timely public health interventions. Both these infections peak during the monsoon season in many parts of India.

Conclusion:

High degree of suspicion for coinfections has to be made in patients presenting with febrile illness in tropics in postmonsoon season with deranged laboratory parameters and not responding to therapy. Early screening in suspected cases will help in initiating appropriate treatment and reduce the increased morbidity & mortality associated with these coinfections.

Fig: Distribution of Dengue and scrub coinfection.

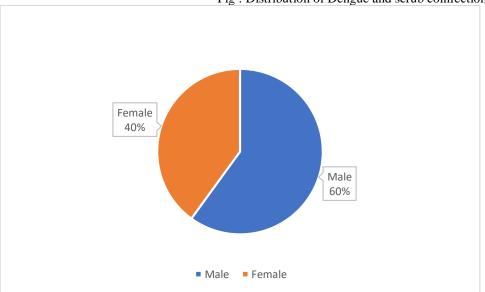


Table 1: Clinicodemographic profile of coinfection

Clinical presentation	Number (percentage)
Fever with chills	15 (100%)
Myalgia	15 (100%)
Rash	7 (46.67%)
Lymphadenopathy	7 (46.67%)
cough	7 (46.67%)
Jaundice	5 (33.33%)
Abdominal pain	5 (33.33%)
Altered sensorium	4 (26.67%)
Diarrhoea	3 (20%)
Vomiting	2 (13.33%)
Hepatosplenomegaly	2 (13.33%)

Table-2: Laboratory parameters with coinfection

Altered blood sodium level	3 (20%)
Hypocalcemia	4 (26.67%)
ALT (SGPT) raised	6 (40%)
AST (SGOT) raised	7 (46.67%)
Serum Protein and albumin	Within Normal range

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