ORIGINAL ARTICLE

Burden of Dengue–Typhoid Coinfection in Pediatric Patients: A 6-year Experience from a Tertiary Care Center

Aravinda Anjana[1], Ranjeeta Adhikary[2], Malavalli V Bhavana[3]

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Abstract

Background: India is endemic to both typhoid and dengue, which also mimic in their clinical presentations. This poses a diagnostic dilemma especially for pediatric patients. Literature on such coinfections is limited.

Methodology: We retrospectively analyzed six years data (2017–2022). All pediatric culture proven typhoid cases with concurrent dengue infection were included in the study. Patient clinical and demographic profiles were extracted from the hospital information system.

Results: We report four such cases of coinfection. Along with the expected reduced platelet counts, most of the patients had associated deranged TLC, liver enzymes, hypoalbuminemia and gallbladder changes.

Conclusion: Our study contributes to the body of literature on dengue–typhoid coinfection in pediatric patients and the pitfall in accepting a single pathogen etiology. Awareness needs to be raised among healthcare workers on the potential dengue–typhoid coinfection, especially in endemic countries.

Keywords: Coinfection, Dengue, Typhoid.

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Background

Dengue, the arthropod-borne systemic viral infection that is ubiquitous in tropical and subtropical climates worldwide, has always been a growing challenge to public health officials. It is estimated as high as 390 million dengue virus (DENV) infections/year, of which only 17–35% manifests clinically, and 70% of the actual burden is in Asia.[1] DENV in humans is often apparent, leading to a wide range of clinical manifestations, from mild fever to potentially fatal dengue shock syndrome. Typhoid fever, a foodborne infection mostly characterized by fever and abdominal pain, is caused by the dissemination of *Salmonella enterica* serovar Typhi or Paratyphi, for which humans are the only hosts. Typhoid cases have been reported between 12 and 21 million cases and over 140,000 deaths each year globally. Without effective treatment, it has a case-fatality rate of 10–30%.[2,3]

Not only are they both endemic in India, but they also mimic clinical presentation, hence posing a diagnostic challenge, especially in pediatric patients. Clinicians need to be well aware of the potential for concurrent typhoid fever when treating patients with dengue infection. There are only a few sporadic case reports of coinfection of dengue with typhoid.[4,5] We hereby present four cases of dengue–typhoid coinfection reported in pediatric patients from our hospital over the last 6 years.

Materials and Methods

We have done a retrospective analysis of blood culture-proven pediatric typhoid cases concurrently diagnosed with dengue infection by serology [NS1 and/or immunoglobulin M (IgM) reactive] from 2017 to 2022. Only patients with ages ≤17 years were included. For blood culture, samples were collected in BACT/ALERT 3D (bioMérieux, France) bottles and incubated for 5 days. When flashed positive, direct Gram staining was performed from the bottle and then subcultured onto blood and MacConkey agar. From the pure bacterial colonies, it was further processed for final identification and antibacterial susceptibility testing by conventional and/or automated VITEK-2 compact (bioMérieux, France) platform and interpreted following the Clinical and Laboratory Standards Institute guidelines.[6] Dengue serology was performed by enzyme-linked immunosorbent assay (ELISA) using BIO-RAD Platelia™ Dengue NS1 antigen (France) and Abbott Dengue IgM Capture ELISA (Korea). False positive IgM due to cross-reactive rheumatoid factor was ruled out. Patient demographic and clinical and radiologic profiles are extracted from the hospital information system. We have compiled the relevant laboratory and clinical parameters as summarized in Table 1.

Results

There were four cases of coinfection, all hailed from Karnataka, India, with ages ranging from 2 to 17 years. Presenting symptoms were primarily high-grade fever >3 days and myalgia with/without gastrointestinal symptoms. All were admitted with a length of stay ranging from 4 to 7 days. None of the patients had rashes. Blood investigations revealed elevated liver enzymes, deranged total leucocyte count (TLC), and hypoalbuminemia. Three patients had

[1–3]Department of Laboratory Medicine, Manipal Hospitals, Bengaluru, Karnataka, India

Corresponding Author: Aravinda Anjana, Department of Laboratory Medicine, Manipal Hospitals, Bengaluru, Karnataka, India, Phone: +91 9560348696, e-mail: anjoo.prabhu@gmail.com

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Table 1: Compiled data on clinical and laboratory parameters

Sl. No	*Gender*	*Age (years)*	*Clinical presentation*	*Length of stay (days)*	*Dengue serology*	*Blood culture*	*Relevant blood parameters*	*Radiology*	*Treatment*
1	Female	6	Fever associated with loose stools, vomiting for 6 days	7	IgM reactive	*S.* Typhi isolated	AST/ALT: 143/65 IU/mL TLC: 17,910/mm^3 PC: 71,000/mm^3 Hb: 10.2 gm/dL Serum alb: 2.6 gm/dL	• Gallbladder wall edema. • Mild splenomegaly. • Mild ascites with bilateral minimal pleural effusion. • Mesenteric lymphadenopathy.	Inj. ceftriaxone
2	Female	2	High-grade fever for 5 days, with associated abdominal distension	5	IgM reactive	*S.* Typhi isolated	AST/ALT: 65/43 IU/mL PC: 115,000/mm^3 Hb: 6.8 gm/dL Serum alb: 2.8 gm/dL	• Mild gallbladder wall edema. • Mild ascites with mild right pleural effusion.	Inj. ceftriaxone
3	Male	4	High-grade fever, vomiting, and loose stools for 3 days Tender hepatomegaly on palpation	4	IgM reactive	*S.* Typhi isolated	AST/ALT: 78/41 IU/mL TLC: 2240/mm^3 PC: 66,000/mm^3 Hb: 10 gm/dL Serum alb: 3.2 gm/dL	Not done	Inj. ceftriaxone
4	Male	17	Fever headache and generalized weakness	5	NS1 reactive	*S.* Typhi isolated	AST/ALT: 30/22 IU/mL TLC: 3800/mm^3 PC: 92,000/mm^3 Hb: 12.7 gm/dL Serum alb: 4.4 gm/dL	Splenomegaly	Inj. ceftriaxone

AST, aspartate aminotransferase; ALT, alanine aminotransferase; TLC, total leucocyte count; PC, platelet count; Hb, hemoglobin; Alb, albumin

platelet counts (PCs) <100,000/mm^3. Clinical and/or radiological organomegaly with gallbladder wall edema were elicited. Blood culture grew *S.* Typhi in all four cases; all were susceptible to azithromycin, ceftriaxone, and trimethoprim/sulfamethoxazole. One isolate was resistant against ciprofloxacin while the other three were intermediately susceptible. Dengue was diagnosed by IgM reactivity in three and by NS1 positivity in one.

Accordingly, the patients were started on injection (inj.) ceftriaxone along with other supportive measures and recovered without any complications. One case was a relapse case of typhoid, who was diagnosed and treated for the same elsewhere with a history of asymptomatic phase for 10 days before presenting to us. Possible malaria coinfection was ruled out in all the cases. None of the patients in the present study presented hemorrhagic manifestations against DENV. There were no associated comorbidities except for one who had associated iron deficiency anemia.

Discussion

Both dengue and typhoid fever are notifiable diseases in India, known to be increasingly reported during the monsoons.[7,8] Vigna et al. published a case report on two such patients who also presented with high-grade fever, myalgia, and gastrointestinal symptoms: nausea, vomiting, and abdominal pain. Such symptoms can be seen in both typhoids and the "dengue with warning signs" group of patients.[8] If not diagnosed and treated promptly, both dengue and typhoid can progress into complications such as septic shock and multiorgan failure. Given that both typhoid fever and dengue fever are endemic in India, coinfection should always be kept in mind while dealing with cases of dengue or typhoid with or without atypical features.[4] Among the available few Indian studies, coinfection rate as high as 34 and 7.8% have been seen among acute febrile illness patients.[7,9] Bhatti et al. has reported false positive results for *S.* Typhi IgM during the febrile phase of DENV infection, which were culture negatives for typhoid.[10] Hence, in our study, we have included only culture-proven typhoid cases.

The present study is a retrospective analysis limited to a small geographical region of Southern India. It may actually be the representative of the tip of the iceberg of the underlying burden. Not all such cases of acute febrile illnesses are being tested for other possible co-pathogens and mostly end up diagnosing a single pathogen etiology. There is a high likelihood of underdiagnosing such concurrent infection as the real incidence is unknown. We found that along with the expected reduced PCs, most of the patients had associated deranged TLC, liver enzymes, hypoalbuminemia, and gallbladder changes. But, there is the scope of immense work on the study of developing the risk factor predictors of such coinfections in the pediatric age group, which will be immensely useful in areas where dengue outbreaks occur in the background of high transmission of endemic infections.[5] Limitation of the present study is less number of cases to make an association. Hence, a further detailed study is required to determine the real incidence of coinfection in order to improve the management of acute febrile illness. In order to reduce the burden of disease, along with the improvement of sanitation and personal hygiene, emphasis should be given to vaccination against typhoid.[7]

Conclusion

The present study contributes to the body of literature on the coinfection between dengue and typhoid fever in pediatric patients

and the pitfall in accepting a single diagnosis. Such coinfections are not uncommon. Awareness needs to be raised among health care workers on the possibility of such coinfections, especially in endemic countries like India.

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