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Dengue viral illness and its co-infection with typhoid fever: a diagnostic dilemma. A study from tertiary care hospital, Uttarakhand.

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Abstract

Background: Dengue and typhoid fever are among the commonest causes of acute febrile illnesses with overlapping signs and symptoms. These dual infections create a diagnostic dilemma which delays prompt diagnosis and treatment especially in endemic areas during monsoon season. The present study is aimed to determine the prevalence of dengue fever at a tertiary care hospital during monsoon period and its co-infection with Typhoid fever.

Materials and Methods: This retrospective observational study was done from July-November 2022 at GBCM and associated Dr. KKBM Subharti hospital after approval from ethical committee. The diagnosis of Dengue fever was done on basis of clinical findings along with positive immune-chromatography based tests detecting NS1 antigen with or without IgM antibodies. Serodiagnosis of Salmonella infection was done through IgM immune-chromatographic tests along with Tube-widal test and blood culture.

Statistical analysis: Descriptive statistics are expressed as mean (± SD) and comparisons of categorical variables used the Chi-square test and fisher exact p test. A p-value ≤0.05 was considered significant. Results are expressed in percentage where required.

Results: Out of total 1960 febrile sera samples tested,204 were tested positive for Dengue, and 671were tested positive for typhoid fever respectively. Maximum number of dengue cases were seen during month of November (34.8%) whereas, co-infection cases were maximum in august (41.1%) Female outnumbered males in both dengue and co-infection cases with M:F ratio being 1.3:1. The mean age was 29.65 ± 11.36 years (range: 03-67 years) with peak number of cases in age group 21-40 years. Out of 34 samples with co-infection,88.2 % samples with S.typhi IgM positive cases showed significant titres {titre o and/or H/AH >/=160} in

tube widal test. Case Fatality Rate (CFR) in dengue cases and co-infection cases was zero. Blood cultures were negative for all dengue and typhoid co-infection cases. Patients testing positive for both NS1Ag and anti-D IgM were significantly more likely to test positive for S. Typhi IgM as compared with only NS1 or IgM dengue cases. ($p<.0001$)

Conclusion: Presence of dual infections should always be kept in mind while dealing with cases of febrile illnesses especially during rainy season. Accurate and early diagnosis is required in such cases to reduce morbidity and mortality. Improvement of sanitation and personal hygiene along with vaccination against typhoid should be promoted along with 4 s of dengue preventive measures (search and destroy mosquito breeding places, self-protective measures, support fogging and seeking early consultation.

Keywords: Dengue fever, Acute febrile illness, Typhoid fever, Rapid card tests, co-infection

Introduction

Acute febrile illness (AFI) is a common clinical syndrome caused by dengue, typhoid, Japanese Encephalitis, Chikungunya, Leptospirosis, Influenza and Malaria [1]. Dengue viral illness caused by the arbovirus and transmitted via Aedes aegypti mosquitoes usually presents with high grade fever, generalized body ache, nausea with or without vomiting. Typhoid fever is a bacterial disease caused by Salmonella spp. transmitted through faeco-oral route and has similar symptoms [2]. Dengue and typhoid fever, if not approached timely, may lead to life threatening complications [3-5]. The major symptoms are common to all these febrile illnesses and non-specific, thus makes it difficult to differentiate from numerous other febrile illnesses of viral or bacterial origin [6-7]. Usually, acute febrile illness is known to be caused by a single etiologic agent. However, recently many articles and case reports are documenting dual infections [8-10]. Co-infections can occur either due to host related factors or vector adaptability as in the case of dengue and chikungunya [11,12]. The other reason might be environmental factors or agent related factors as in the association of typhoid fever with polio virus [13]. We believe that increasingly infectious diseases are presenting with atypical manifestations or as dual infections. There is a need to document such cases which could improve awareness among clinicians for the changing dynamics of disease manifestations. These patients often gets benefitted from specific diagnostic laboratory studies for dengue and other infectious organisms endemic to the region [14-15]. Dengue co-infection with malaria and other febrile illness have been studied widely, but there is paucity of data relevant to the dengue and typhoid co-infection from Uttarakhand region as both dengue and typhoid fever are endemic in this area. The present study was designed to explore the prevalence of dengue fever in febrile patients and its co-infection with typhoid fever.

Materials and methods

A retrospective analysis was done between July and November 2022 in department of Microbiology at Gautam Buddha Chikitsa Mahavidhyalaya (GBCM) and associated Dr. KKBM subharti hospital (800 bedded tertiary care hospital situated in Dehradun, Uttarakhand. The study was approved by our ethical committee. IEC number provided is GBCM/IEC/2023/07-02. Dengue viral infection was diagnosed by $NS1_{Ag}$ and/or anti-D IgM antibodies positivity by card test (Rapi GEN BIOCREDIT dengue NS1Ag+Ab Duo) along with decrease in platelet (platelet count less than 1.5 lakh per microlitre) count. Serodiagnosis of Salmonella typhi infection was conducted by rapid card (Typhoid IgG/IgM Rapid Test, Biocan Diagnostics Inc., Canada) along with

tube widal test which is a tube agglutination test and detects antibodies against O and H antigens of salmonella typhi and H antigens of salmonella paratyphi A and B. Titre value of ≥1:160 for both O and H was considered as clinically significant in single acute phase samples. Demographic data including age, sex and detailed history of onset of symptoms were recorded from medical records. Patients with anti-D IgG on initial screen were excluded from this analysis. Blood cultures were also done for co-infected cases.

Results

A total of 204 (10.4%) cases were found to be positive for dengue among samples tested for febrile illnesses. Among which 94/204 for $NS1_{Ag}$ (46.07%),78/204 (38.23%) for IgM and 32/204 (15.7%) for Ns1 with IgM. Of all 204 patients with DVI, 34 (16.7%) tested positive for S. Typhi IgM. Out of 34 samples, thirty (79%) samples showed significant titres in tube-widal test. In both dengue cases and co-infection cases, females outnumbered males. Female to male ratio is found to be 1.3:1 [Figure 1]. August was the peak month for co-infection cases (41.1%) whereas, dengue cases were maximum seen during month of November (34.8%) [Table 2]. Peak age group was 21-40 years (51.4 %) with least in above 60yrs (7.8%) of age group [Table 1]. The mean age was found to be 29.65 ± 11.36 years (range: 03-67 years) Majority of laboratory parameters in all febrile illnesses were thrombocytopenia (91.2%), hepatic dysfunction (49%), and leukopenia (35%). Blood culture were negative for all the co-infected cases. Only 4/34 no of samples (positive for dengue Ns1ag/+-IgM and salmonella typhi IgM) showed insignificant titres (O and H </= 80) in tube widal test and were not considered as co-infection cases. Patients testing positive for both NS1Ag and anti-D IgM were significantly more likely to test positive for S. Typhi IgM as compared with only NS1 or IgM dengue cases. (p<.0001) [Table 3].

Discussion

Prevalence of dengue in monsoon season among febrile illnesses in our study is found to be 10.4 % which is comparatively less 38.2% and 21.39% as compared with study by Chauhan et al and Sharma et al respectively [2,14]. Large number of samples tested for febrile illnesses at our institute along with lack of similar studies in recent years in this region might be the cause. Mean age group in our study is found to be 29.6+-11.36 years with Male: Female ratio being 1:1.3. Females outnumbered males. This is in contrast with many studies who have found males affected more than females [15]. Although, study by Mahato et al supports ours by their female preponderance in the study group [16]. Female gender acquires infection easily preparation of food and other activities like cleaning with contaminated water and childcare. This might have increased the frequency of dengue and typhoid co-infection in females. Maximum patients were from the age group of 21-40 years. This may be because of working age group and their relative more exposure to external environment. The rate of co-infection in present study is 14.7% which is much higher than many other earlier studies. Kasper et al, and another study from South India reported rates of co-infection to as low as 0.3% and 0.6% respectively [17-18]. However, in a study from New Delhi and Uttar Pradesh, the rate of co-infection was as high as in the present study. They reported a rate of 7.8%. It is a known fact that viral illnesses are followed by bacteria infections especially in upper respiratory diseases. The predisposing factors of salmonella infection in dengue fever might be due to hemodynamic and inflammatory changes during rainy season.

Those patients with positive results for both NS1Ag and anti-D IgM for dengue were significantly more likely to have positive test for S. typhi IgM compared to patients testing positive for either Ns1 or IgM for both which was statically significant with p value <0.0001. Previous antibiotic status was unknown for all the patients, so negative blood cultures were not considered in account. Almost all the samples except four tested positive for both dengue and typhoid fever showed significant titres in tube-widal test. Insignificant titres with positive IgM antibodies for Salmonella typhi creates a strong suspicion of cross reactivity between these two febrile illnesses which were also supported by study by Bhatti et al [19]. No other data regarding cross reactivity of rapid immunoassays are documented till date besides this study.

Conclusion

During rainy season (July-November), drinking water gets contaminated easily due to inadequate sanitation systems in most of the regions as well as it is a breeding season for mosquitoes [20-22]. Accurate and timely diagnosis and management of Dengue fever and its co-infection with typhoid fever and other illnesses is essential in order to avoid life- threatening complications. Emphasis on good sanitation systems with typhoid vaccination should be done. Dengue preventive measures such as self- protection by wearing full sleeves clothes, search and destroy the breeding areas, frequent spraying defogging with insecticides and early seeking medical care should be emphasized.

In our study, we conclude that prevalence of dengue viral illnesses is high during monsoon season and co-infection between dengue and typhoid fever is quite common and on rising trend. Thus, it should always be kept in mind while treating acute febrile illnesses.

Limitation

The diagnosis of Dengue fever could have been done by viral culture, molecular techniques, or immune-essays testing but it was not possible at our newly setup tertiary care hospital due to limited resources. Serum samples are stored for further study at -20 degree temperature.

References

1. Capeding MR, Chua MN, Hadine Goro SR, et al. Dengue and other common causes of acute febrile illness in Asia: an active surveillance study in children. PLOS Neg Trop Dis. 2013;7(7): e2331. [PMC free article] [PubMed] [Google Scholar]
2. Sharma Y, Arya V, Jain S, Kumar M, Deka L, Mathur A. Dengue and typhoid co-infection– Study from a Government Hospital in North Delhi. J Clin Diagn Res. 2014; 8: 09-11.
3. Chrispal A, Boorugu H, Gopinath K, et al. Acute undifferentiated febrile illness in adult hospitalized patients: the disease spectrum and diagnostic predictors – an experience from a tertiary care hospital in South India. Trop Doct. 2010;40(4):230–34. [PubMed] [Google Scholar]
4. Buckle GC, Walker CL, Black RE. Typhoid fever and paratyphoid fever: systematic review to estimate global morbidity and mortality for 2010. J Glob Health. 2012 Jun; 2(1): 010401. doi: 10.7189/jogh. 01.010401. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
5. Green S, Rothman A. Immunopathological mechanisms in dengue and dengue hemorrhagic fever. Curr Opin Infect Dis. 2006 Oct;19(5):429–36. doi: 10.1097/01.qco.0000244047.31135.fa.[PubMed] [CrossRef] [Google Scholar]
6. Concurrent dengue hemorrhagic fever and typhoid fever infection in adult: Case report. Sudjana P, Jusuf

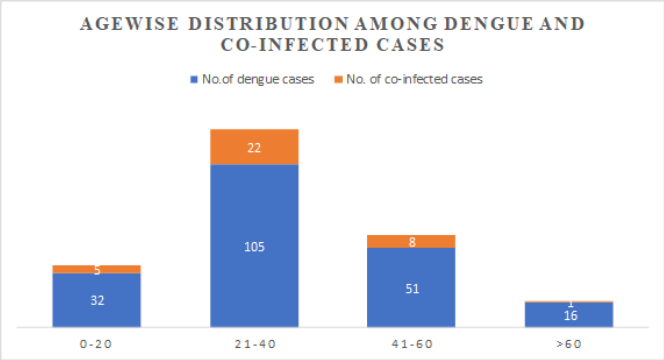
H. Southeast Asian J Trop Med Public Health. 1998;29:370–372. [PubMed] [Google Scholar]

7. Ganeshkumar P, Murhekar MV, Poornima V, Saravanakumar V, Sukumaran K, Anandaselvasankar A, et al. Dengue infection in India: A systematic review and meta-analysis. PloS Neglect Tropical Dis. 2018;12(7):e0006618.
8. Bhalla A, Sharma N, Sharma A, Suri V. Concurrent infection with dengue and malaria. Indian J Med Sci 2006 Aug;60(8):330–1. [CrossRef] [Pubmed] Basuki PS. Concurrent dengue infection and enteric fever. a case series. Folia Medica Indonesiana 2003 Mar;39(1):54–60.
9. Bansal R, Bansal P, Tomar LR. Typhoid and dengue coinfection: case reports. Trop Doct 2015 Jan;45(1):52–3. [CrossRef] [Pubmed
10. Chahar HS, Bharaj P, Dar L, Guleria R, Kabra SK, Broor S. Co-infections with chikungunya virus and dengue virus in Delhi, India. Emerg Infect Dis 2009 Jul;15(7):1077–80 [CrossRef] [Pubmed]
11. Mandell GL, Bennett JE, Dolin R, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 7ed. Philadelphia: Churchill Livingstone; 2010.
12. Dikid T, Jain SK, Sharma A, Kumar A, Narain JP. Emerging & re-emerging infections in India: an overview. Indian J Med Res 2013; 138:19–31. [Pubmed]
13. Chauhan S, Sharma S, Surender Singh P. Morphometric features of asterion in adult human skulls. Int J Res Med Sci 2019;7: 1615-7.
14. Prasith N, Keosavanh O, Phengxay M, Stone S, Lewis HC, Tsuyuoka R, Matsui T, Phongmanay P, Khamphaphongphane B, Arima Y. Assessment of gender distribution in dengue surveillance data, the Lao People's Democratic Republic. Western Pac Surveill Response J. 2013 May 21;4(2):17-24. doi: 10.5365/WPSAR.2012.3.4.020. PMID: 24015367; PMCID: PMC3762968.
15. Mahato AK, Shrestha N, Gharti SB, Shah M. Typhoid Fever among Patients Diagnosed with Dengue in a Tertiary Care Centre: A Descriptive Cross-sectional Study. JNMA J Nepal Med Assoc. 2022 Aug;60(252):714–7. doi: 10.31729/jnma.7624. Epub 2022 Aug 31. PMCID: PMC9446503.
16. Kasper MR, Blair PJ, Touch S, Sokhal B, Yasuda CY, Williams M, et al. Infectious etiologies of acute febrile illness among patients seeking health care in south-central Cambodia. Am J Tropical Med Hygiene. 2012;86(2):246-53Buchy P, Peeling R. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. Geneva: WHO; 2009. Laboratory diagnosis and diagnostic tests; pp. 91–107. [Google Scholar]
17. Kamath SR, Ranjit S. Clinical features, complications and atypical manifestations of children with severe forms of dengue haemorrhagic fever in South India. Indian J Pediat. 2006;73(10):889-95.
18. Bhatti AB, Ali F, Satti SA. Cross-Reactivity of Rapid Salmonella Typhi IgM Immunoassay in Dengue Fever Without Co-Existing Infection. Cureus. 2015 Dec 4;7(12):e396. doi: 10.7759/cureus.396. PMID: 26798572; PMCID: PMC4699986.
19. Ashish B, Navneet S, Aman S, Vikas S. Letter to editor-concurrent infection with dengue and malaria. Indian journal of medical sciences. 2006 Aug 1;60(8):330–1. doi: 10.4103/0019-5359.26610. [PubMed] [CrossRef] [Google Scholar]
20. Mushtaq MB, Qadri MI, Rashid A. Concurrent infection with dengue and malaria: an unusual presentation. Case reports in medicine. 2013 Mar

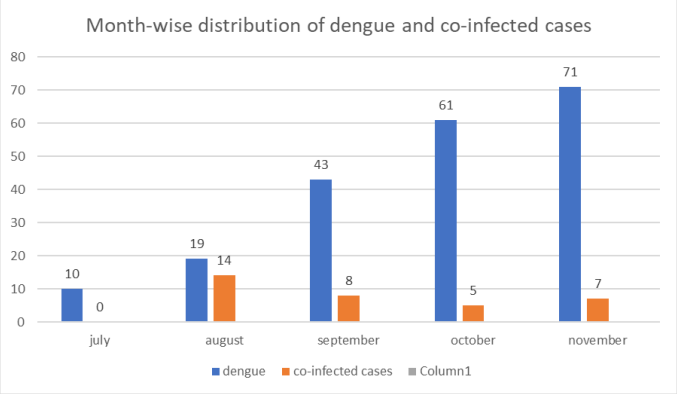
30;2013:520181. doi: 10.1155/2013/520181. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

21. Basuki PS. Concurrent dengue infection and enteric fever. A case series. Folia Medica Indonesiana. 2003 Jan;39(1):54. [Google Scholar]

Legend Graph and Tables



Graph 1: Age-wise distribution among dengue and co-infected cases



Graph 2 : Monthwise distribution of dengue and co-infected cases

Table 1: Probability of Dengue NS1 ag with or without IgM with Typhoid IgM cases

	Typhoid IgM positive	Typhoid IgM negative	Fisher exact p test
NS1 Ag positive	10	84	Two tailed value is 0.8142
NS1 Ag negative	10	72	
Dengue IgM positive	6	72	Two tailed value is 0.6031
Dengue IgM negative	10	84	
Both NS1 Ag and Dengue IgM positive	14	18	Two tailed p value <.0001 (extremely significant)
Both NS1 Ag and Dengue IgM negative	16	146	