International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 26-11-2019; Accepted: 27-12-2019
www.medicalsciencejournal.com
Volume 6; Issue 1; January 2020; Page No. 122-126

Study of correlation of dengue fever and enteric fever in childrens in Bihar region

Dr. Ashutosh Kumar[1], Dr. Kripa Nath Mishra[2*]
[1] Senior Resident, Department of Pediatrics, Darbhanga Medical College and Hospital Darbhanga (DMCH), Bihar, India
[2] Professor and HOD, Department of Paediatrics, Darbhanga Medical College and Hospital Darbhanga, Bihar, India
[*] Corresponding Author: Dr. Kripa Nath Mishra

Abstract
In developing countries, infectious diseases contribute considerably to morbidity and mortality. Sometimes concurrent infections with multiple infectious agents may occur, which make the correct diagnosis and management a challenging task. Hence the present study was planned for evaluation of case of co-infection of typhoid fever with dengue fever. Hence based on above finsgins the present study was planned for study of Correlation of Dengue Fever and Enteric Fever in Childrens.
The present study was planned in Department of Pediatrics, Darbhanga Medical College and Hospital Darbhanga, Bihar. Total 25 cases of the Dengue fever were enrolled in the present study. Dengue viral infection was confirmed by observing the platelet count decreased (less than 150000 platelets per microliter of blood) from normal level. Clinical characteristics of Dengue fever patients showed Fever, headache, muscle aches and thrombocytopenia. Apart from the dengue symptoms, patients Co-infected with typhoid fever showed coated tongue, fatigue, Sweating, Dry cough, Loss of appetite and weight loss and abdominal pain. The patient serum was tested for Dengue virus NS1 and/or IgM samples. The Widal test used for the antibody titer and titer value of >1:80 considered as clinically significant.
The data generated from the present study concludes that the high prevalence rate of Dengue fever may leads to co-infections with typhoid are common and it should be properly diagnosed and timely medication should be provided to reduce complications and also to avoid mortality.

Keywords: dengue fever, enteric fever, childrens, Bihar region, etc

Introduction
Dengue fever is a mosquito-borne tropical disease caused by the dengue virus. Symptoms typically begin three to fourteen days after infection. These may include a high fever, headache, vomiting, muscle and joint pains, and a characteristic skin rash. Recovery generally takes two to seven days. In a small proportion of cases, the disease develops into severe dengue, also known as dengue hemorrhagic fever, resulting in bleeding, low levels of blood platelets and blood plasma leakage, or into dengue shock syndrome, where dangerously low blood pressure occurs [1].
Dengue is spread by several species of female mosquitoes of the Aedes type, principally A. aegypti. The virus has five types; infection with one type usually gives lifelong immunity to that type, but only short-term immunity to the others. Subsequent infection with a different type increases the risk of severe complications. A number of tests are available to confirm the diagnosis including detecting antibodies to the virus or it's RNA [2].
A vaccine for dengue fever has been approved and is commercially available in a number of countries. The vaccine, however, is only recommended in those who have been previously infected. Other methods of prevention include reducing mosquito habitat and limiting exposure to bites. This may be done by getting rid of or covering standing water and wearing clothing that covers much of the body. Treatment of acute dengue is supportive and includes giving fluid either by mouth or intravenously for mild or moderate disease. For more severe cases, blood transfusion may be required. About half a million people require hospital admission every year. Paracetamol (acetaminophen) is recommended instead of nonsteroidal anti-inflammatory drugs (NSAIDs) for fever reduction and pain relief in dengue due to an increased risk of bleeding from NSAID use [2].
Dengue has become a global problem since the Second World War and is common in more than 120 countries, mainly in Asia and South America. Each year between 50 and 528 million people are infected and approximately 10,000 to 20,000 die. In 2019 a significant increase in the number of cases was seen. The earliest descriptions of an outbreak date from 1779. Its viral cause and spread were understood by the early 20th century. Apart from eliminating the mosquitos, work is ongoing for medication targeted directly at the virus. It is classified as a neglected tropical disease [3].
Typically, people infected with dengue virus are asymptomatic (80%) or have only mild symptoms such as an uncomplicated fever. Others have more severe illness (5%), and in a small proportion it is life-threatening. The incubation period (time between exposure and onset of symptoms) ranges from 3 to 14 days, but most often it is 4 to 7 days. Therefore, travelers returning from endemic areas are unlikely to have dengue if fever or other symptoms start more than 14 days after arriving home. Children often experience symptoms similar to those of the common cold and gastroenteritis (vomiting and diarrhea) and have a greater risk of severe complications, though initial symptoms are generally mild but include high fever [4].
The characteristic symptoms of dengue are sudden-onset

fever, headache (typically located behind the eyes), muscle and joint pains, and a rash. The alternative name for dengue, "breakbone fever", comes from the associated muscle and joint pains. The course of infection is divided into three phases: febrile, critical, and recovery [5].

The febrile phase involves high fever, potentially over 40 °C (104 °F), and is associated with generalized pain and a headache; this usually lasts two to seven days. Nausea and vomiting may also occur. A rash occurs in 50–80% of those with symptoms in the first or second day of symptoms as flushed skin, or later in the course of illness (days 4–7), as a measles-like rash. A rash described as "islands of white in a sea of red" has also been observed. Some petechiae (small red spots that do not disappear when the skin is pressed, which are caused by broken capillaries) can appear at this point, as may some mild bleeding from the mucous membranes of the mouth and nose. The fever itself is classically biphasic or saddleback in nature, breaking and then returning for one or two days [6].

In some people, the disease proceeds to a critical phase as fever resolves. During this period, there is leakage of plasma from the blood vessels, typically lasting one to two days. This may result in fluid accumulation in the chest and abdominal cavity as well as depletion of fluid from the circulation and decreased blood supply to vital organs. There may also be organ dysfunction and severe bleeding, typically from the gastrointestinal tract. Shock (dengue shock syndrome) and hemorrhage (dengue hemorrhagic fever) occur in less than 5% of all cases of dengue; however, those who have previously been infected with other serotypes of dengue virus ("secondary infection") are at an increased risk. This critical phase, while rare, occurs relatively more commonly in children and young adults [4].

The recovery phase occurs next, with resorption of the leaked fluid into the bloodstream. This usually lasts two to three days. The improvement is often striking, and can be accompanied with severe itching and a slow heart rate. Another rash may occur with either a maculopapular or a vasculitic appearance, which is followed by peeling of the skin. During this stage, a fluid overload state may occur; if it affects the brain, it may cause a reduced level of consciousness or seizures. A feeling of fatigue may last for weeks in adults [4].

Dengue fever virus (DENV) is an RNA virus of the family Flaviviridae; genus Flavivirus. Other members of the same genus include yellow fever virus, West Nile virus, Zika virus, St. Louis encephalitis virus, Japanese encephalitis virus, tick-borne encephalitis virus, Kyasanur forest disease virus, and Omsk hemorrhagic fever virus. Most are transmitted by arthropods (mosquitos or ticks), and are therefore also referred to as arboviruses (arthropod-borne viruses).

The dengue virus genome (genetic material) contains about 11,000 nucleotide bases, which code for the three different types of protein molecules (C, prM and E) that form the virus particle and seven other non-structural protein molecules (NS1, NS2a, NS2b, NS3, NS4a, NS4b, NS5) that are found in infected host cells only and are required for replication of the virus. There are five strains of the virus, called serotypes, of which the first four are referred to as DENV-1, DENV-2, DENV-3 and DENV-4. The fifth type was announced in 2013. The distinctions between the serotypes are based on their antigenicity [7].

Dengue virus is primarily transmitted by Aedes mosquitos, particularly A. aegypti. These mosquitos usually live between the latitudes of 35° North and 35° South below an elevation of 1,000 metres (3,300 ft). They typically bite during the early morning and in the evening, but they may bite and thus spread infection at any time of day. Other Aedes species that transmit the disease include A. albopictus, A. polynesiensis and A. scutellaris. Humans are the primary host of the virus, but it also circulates in nonhuman primates. An infection can be acquired via a single bite. A female mosquito that takes a blood meal from a person infected with dengue fever, during the initial 2- to 10-day febrile period, becomes itself infected with the virus in the cells lining its gut. About 8–10 days later, the virus spreads to other tissues including the mosquito's salivary glands and is subsequently released into its saliva. The virus seems to have no detrimental effect on the mosquito, which remains infected for life. Aedes aegypti is particularly involved, as it prefers to lay its eggs in artificial water containers, to live in close proximity to humans, and to feed on people rather than other vertebrates [8].

Dengue can also be transmitted via infected blood products and through organ donation. In countries such as Singapore, where dengue is endemic, the risk is estimated to be between 1.6 and 6 per 10,000 transfusions. Vertical transmission (from mother to child) during pregnancy or at birth has been reported. Other person-to-person modes of transmission, including sexual transmission, have also been reported, but are very unusual. The genetic variation in dengue viruses is region specific, suggestive that establishment into new territories is relatively infrequent, despite dengue emerging in new regions in recent decades [4].

Severe disease is more common in babies and young children, and in contrast to many other infections, it is more common in children who are relatively well nourished. Other risk factors for severe disease include female sex, high body mass index, and viral load. While each serotype can cause the full spectrum of disease, virus strain is a risk factor. Infection with one serotype is thought to produce lifelong immunity to that type, but only short-term protection against the other three. The risk of severe disease from secondary infection increases if someone previously exposed to serotype DENV-1 contracts serotype DENV-2 or DENV-3, or if someone previously exposed to DENV-3 acquires DENV-2. Dengue can be life-threatening in people with chronic diseases such as diabetes and asthma [9].

Polymorphisms (normal variations) in particular genes have been linked with an increased risk of severe dengue complications. Examples include the genes coding for the proteins TNFα, mannan-binding lectin, CTLA4, TGFβ, DC-SIGN, PLCE1, and particular forms of human leukocyte antigen from gene variations of HLA-B. A common genetic abnormality, especially in Africans, known as glucose-6-phosphate dehydrogenase deficiency, appears to increase the risk [48]. Polymorphisms in the genes for the vitamin D receptor and FcγR seem to offer protection against severe disease in secondary dengue infection [9].

When a mosquito carrying dengue virus bites a person, the virus enters the skin together with the mosquito's saliva. It binds to and enters white blood cells, and reproduces inside the cells while they move throughout the body. The white blood cells respond by producing a number of signaling proteins, such as cytokines and interferons, which are responsible for many of the symptoms, such as the fever, the

flu-like symptoms, and the severe pains. In severe infection, the virus production inside the body is greatly increased, and many more organs (such as the liver and the bone marrow) can be affected. Fluid from the bloodstream leaks through the wall of small blood vessels into body cavities due to capillary permeability. As a result, less blood circulates in the blood vessels, and the blood pressure becomes so low that it cannot supply sufficient blood to vital organs. Furthermore, dysfunction of the bone marrow due to infection of the stromal cells leads to reduced numbers of platelets, which are necessary for effective blood clotting; this increases the risk of bleeding, the other major complication of dengue fever [10].

Typhoid fever, also known simply as typhoid, is a bacterial infection due to a specific type of Salmonella that causes symptoms. Symptoms may vary from mild to severe, and usually begin 6 to 30 days after exposure. Often there is a gradual onset of a high fever over several days. This is commonly accompanied by weakness, abdominal pain, constipation, headaches, and mild vomiting. Some people develop a skin rash with rose colored spots. In severe cases, people may experience confusion. Without treatment, symptoms may last weeks or months. Diarrhea is uncommon. Other people may carry the bacterium without being affected; however, they are still able to spread the disease to others. Typhoid fever is a type of enteric fever, along with paratyphoid fever [11].

The cause is the bacterium Salmonella enterica subsp. enterica growing in the intestines and blood. Typhoid is spread by eating or drinking food or water contaminated with the feces of an infected person. Risk factors include poor sanitation and poor hygiene. Those who travel in the developing world are also at risk. Only humans can be infected. Symptoms are similar to those of many other infectious diseases. Diagnosis is by either culturing the bacteria or detecting their DNA in the blood, stool, or bone marrow. Culturing the bacterium can be difficult. Bone-marrow testing is the most accurate [12].

A typhoid vaccine can prevent about 40 to 90% of cases during the first two years. The vaccine may have some effect for up to seven years. For those at high risk or people traveling to areas where the disease is common, vaccination is recommended. Other efforts to prevent the disease include providing clean drinking water, good sanitation, and handwashing. Until an individual's infection is confirmed as cleared, the individual should not prepare food for others. The disease is treated with antibiotics such as azithromycin, fluoroquinolones, or third-generation cephalosporins. Resistance to these antibiotics has been developing, which has made treatment of the disease more difficult [13].

In 2015, 12.5 million new cases worldwide were reported. The disease is most common in India. Children are most commonly affected. Rates of disease decreased in the developed world in the 1940s as a result of improved sanitation and use of antibiotics to treat the disease. Each year in the United States, about 400 cases are reported and the disease occurs in an estimated 6,000 people. In 2015, it resulted in about 149,000 deaths worldwide – down from 181,000 in 1990 (about 0.3% of the global total). The risk of death may be as high as 20% without treatment. With treatment, it is between 1 and 4%. Typhus is a different disease. However, the name typhoid means "resembling typhus" due to the similarity in symptoms.

In developing countries, infectious diseases contribute considerably to morbidity and mortality. Sometimes concurrent infections with multiple infectious agents may occur, which make the correct diagnosis and management a challenging task. Hence the present study was planned for evaluation of case of co-infection of typhoid fever with dengue fever. Hence based on above finsgins the present study was planned for study of Correlation of Dengue Fever and Enteric Fever in Childrens.

Methodology

The present study was planned in Department of Pediatrics, Darbhanga Medical College and Hospital Darbhanga, Bihar. Total 25 cases of the Dengue fever were enrolled in the present study. Dengue viral infection was confirmed by observing the platelet count decreased (less than 150000 platelets per microliter of blood) from normal level. Clinical characteristics of Dengue fever patients showed Fever, headache, muscle aches and thrombocytopenia. Apart from the dengue symptoms, patients Co-infected with typhoid fever showed coated tongue, fatigue, Sweating, Dry cough, Loss of appetite and weight loss and abdominal pain. The patient serum was tested for Dengue virus NS1 and/or IgM samples. The Widal test used for the antibody titer and titer value of >1:80 considered as clinically significant.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Results & Discussion

Like dengue fever, the enteric fever typhoid is endemic in India with same symptoms of febrile illness as like's dengue fever. The global annual burden was estimated at approximately 22 million cases and fatality rate remains at about 1% such that about 222000 typhoid related deaths occur annually [14]. Co-infections with different infectious agents at a time are also becoming a major health problem and similarity of symptoms further makes difficult in accurate clinical diagnosis and treatment. If dengue and typhoid fever is not properly diagnosed may results in life threatening consequences. Dengue Co-infection with malaria and other febrile illness, course of infections have been studied widely [15, 18],

Worldwide, 2.5 billion people live in countries where dengue is endemic and are at a risk of contracting dengue fever or dengue hemorrhagic fever. Of them, 1.3 billion live in 10 countries in the WHO South-East Asia region [19]. Dengue is an important emerging infectious disease in India. In the acute phase of the illness, the clinical features of dengue infection are difficult to distinguish from other illnesses found in tropical areas [19, 20]. Typhoid fever is also common in the 5- to 15-year-old age group, and the reported overall incidence rate of typhoid fever is 214.2 per 100,000 individuals/year [21]. Typhoid fever usually presents with prolonged fever with spikes in temperature without returning to normal. The fever rises in increments and usually reaches 40–40.5°C by the end of the first week of illness. Particularly in dengue, there is a sudden sharp rise in temperature between 39°C and 40°C, and this is frequently accompanied by a flushed face and headache. The fever may be biphasic, lasting 5–7 days in the majority of cases. It is generally an acute febrile illness associated with a severe headache, myalgia, arthralgia, and rashes. In typhoid fever, a dull, continuous frontal headache beginning during the

first 2 days of fever may occur along with gastrointestinal symptoms, such as diarrhea and constipation [22]. In dengue, the critical phase of dengue hemorrhagic fever begins around the time of transition from the febrile to afebrile phase.

Table 1: Demographic Details

Parameters	No. of Cases
Sex	
Males	17
Females	8
Age	
1 – 3 years	6
3 – 6 years	3
6 – 9 years	4
9 – 12 years	5
12 – 15 years	7
Total Cases	25

Table 2: Dengue Fever Cases with Enteric Fever

Parameters	No. of Cases
Dengue Fever	25
Enteric Fever	8

Children with dengue frequently have upper respiratory symptoms due to concurrent infection with other viruses and bacteria [25]. However, fever persisted in our patient despite signs of recovery from dengue, such as the maintainance of normal blood pressure and improvement in platelet count. According to the WHO, a fever usually lasts for 2–7 days in patients with dengue [23, 24]. However, our patient continued to have fever for >10 days, prompting us to re sevaluate him. His blood culture grew S. typhi on subcultures, and the Widal test results were positive. The first case of coinfection with dengue and typhoid was reported by Sudjana and Jusuf [23]. In a study by Kasper *et al*. [26] from Cambodia, of the 883 cases of dengue infection, 3 (0.30%) had coinfection with typhoid fever. A study by Baba *et al*. [27] from Nigeria reported dengue coinfection with typhoid fever in 13 (4.1%) of 310 febrile patients. A study conducted in Delhi reported dengue– typhoid coinfection in 7.8% of their dengue cases. Although the causal mechanisms remain to be elucidated, dengue virus can cause a diminished T-cell proliferation in response to mitogens in vitro. The breakdown of the intestinal mucosal barrier in dengue may be another reason for increased gram-negative sepsis [26].

Typhoid fever is endemic in India and it is most prevalent in urban areas, with incidence approaching one percent of the population annually in some endemic areas. In the age group between 5 and 15 years the reported incidence of typhoid fever is 214.2 per 100,000/year [28]. In India, dengue virus causes epidemic and sporadic cases year-round, with a peak in frequency from August to November, during the humid season [4]. Co-infections with common endemic pathogens can prove to be a diagnostic challenge especially during dengue outbreaks. Many co-infections with dengue have been reported from tropical countries including malaria, melioidosis and chikungunya. Dual infections with other endemic diseases, such as leptospirosis, viral hepatitis B also have been reported in cases with unusual manifestation [29].

The reasons for bacterial co-infections in some patients with dengue are also not yet fully known. It is known that dengue virus can cause a diminished T cell proliferation in response to mitogens in vitro [31]. However, the in vivo effects of these observations have not been studied. With increasing reports of coinfections in patients with dengue, it would be worthwhile to study the immune effects of dengue in vivo (eg. delayed type hypersensitivity to purified protein derivative). Another probable reason cited for increased gram negative sepsis with dengue is the breakdown of intestinal mucosal barrier [30].

Attempts have been made to identify risk factors predicting presence of bacterial co-infection in adult patients with dengue [16], but similar studies have to be done in pediatric age group.

Conclusion

The data generated from the present study concludes that the high prevalence rate of Dengue fever may leads to co-infections with typhoid are common and it should be properly diagnosed and timely medication should be provided to reduce complications and also to avoid mortality.

References

1. "Dengue and severe dengue Fact sheet N°117". WHO. May 2015. Archived from the original on 2 September, 2016. Retrieved 3 February 2016.
2. Kularatne SA (September 2015). "Dengue fever". BMJ. 351: h4661. doi:10.1136/bmj.h4661. PMID 26374064.
3. "Neglected Tropical Diseases". Cdc.gov. 6 June 2011. Archived from the original on 4 December, 2014. Retrieved 28 November 2014.
4. Simmons CP, Farrar JJ, Nguyen VV, Wills B. "Dengue" (PDF). The New England Journal of Medicine. 2012; 366(15):1423-32. doi:10.1056/NEJMra1110265. hdl:11343/191104. PMID 22494122.
5. WHO, 2009, 25-27. https://en.wikipedia.org/ wiki/ Dengue_fever #refWHO2009
6. Knoop KJ, Stack LB, Storrow A, Thurman RJ. eds. "Tropical medicine". Atlas of emergency medicine (3rd ed.). New York: McGraw-Hill Professional, 2010, pp. 658-9. ISBN 978-0-07-149618-6.
7. Solomonides Tony. Healthgrid applications and core technologies: proceedings of HealthGrid 2010 ([Online-Ausg.]. ed.). Amsterdam: IOS Press, 2010, p. 235. ISBN 978-1-60750-582-2. Archived from the original on 1 May 2016.
8. Gubler DJ "Dengue viruses". In Mahy BWJ; Van Regenmortel MHV (eds.). Desk Encyclopedia of Human and Medical Virology. Boston: Academic Press, 2010, pp. 372-82. ISBN 978-0-12-375147-8. Archived from the original on 9 June 2016.
9. Guzman MG, Halstead SB, Artsob H, Buchy P, Farrar J, Gubler DJ, Hunsperger E, Kroeger A, Margolis HS, Martínez E, Nathan MB, *et al*. "Dengue: a continuing global threat". Nature Reviews. Microbiology. 2010; 8(12 Suppl):S7-16. doi:10.1038/nrmicro2460. PMC 4333201. PMID 21079655.
10. Martina BE, Koraka P, Osterhaus AD. "Dengue virus pathogenesis: an integrated view". Clinical Microbiology Reviews. 2009; 22(4):564-81. doi:10.1128/CMR.00035-09. PMC 2772360. PMID 19822889.
11. Wain J, Hendriksen RS, Mikoleit ML, Keddy KH, Ochiai RL. "Typhoid fever". Lancet. 2015;

385(9973):1136-45. doi:10.1016/s0140-6736(13)62708-7. PMID 25458731.
12. Crump JA, Mintz ED. "Global trends in typhoid and paratyphoid Fever". Clinical Infectious Diseases. 2010; 50(2):241-6. doi:10.1086/649541. PMC 2798017. PMID 20014951.
13. "Oxford English Dictionary (Online)". p. typhoid, adj. and n. Archived from the original on 11 January, 2008. Retrieved 28 March 2015. Resembling or characteristic of typhus.
14. 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; 2:010401.
15. 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.
16. Zaki SA. Malaria and dengue co-infection. Ann Indian Acad Neurol, 2011; 14:141-142.
17. Wiwanitkit V. Concurrent malaria and dengue infection: A brief summary and comment. Asian Pac J Trop Biomed, 2011; 1:326-327.
18. Raut C, Rao N, Sinha D, Hanumaiah H, Manjunatha M. Chikungunya, dengue, and malaria co-infection after travel to Nigeria, India. Emerg Infect Dis, 2015; 21:907-909.
19. Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic Fever Revised and expanded edition © World Health Organization, 2011. Printed in India. Available from: URL: http://www.searo.who. int/entity/vector_borne_tropical_diseases/documents/ SEAROTPS60/en/
20. Basuki PS. Concurrent dengue infection and enteric fever. A case series. Folia Medica Indonesiana, 2003; 39:54-60.
21. Srinivasaraghavan R, Narayanan P, Kanimozhi T. Culture proven Salmonella typhi co-infection in a child with Dengue fever: a case report. J Infect Dev Ctries, 2015; 9:1033-5.
22. Sharma Y, Arya V, Jain S, Kumar M, Deka L, Mathur A, *et al*. Dengue and Typhoid Co-infection–Study from a Government Hospital in North Delhi. J Clin Diagn Res, 2014; 8:9-11.
23. Sudjana P, Jusuf H. Concurrent dengue hemorrhagic fever and typhoid fever infection in adult: case report. Southeast Asian J Trop Med Public Health, 1998; 29:370-72.
24. Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic Fever Revised and expanded edition © World Health Organization, 2011. Printed in India. Available from: URL: http://www.searo.who. int/entity/vector_borne_tropical_diseases/documents/S EAROTPS60/en/
25. Basuki PS. Concurrent dengue infection and enteric fever. Acase series. Folia Medica Indonesiana, 2003; 39:54-60.
26. Kasper RM, Blair JP, Touch S, *et al*. Infectious etiologies of acute febrile illness among patients seeking health care in south-central cambodia. J Trop Med Hyg, 2012; 86:246-53 [CrossRef].
27. Baba M, Logue CH, Oderinde B, *et al*. Evidence of arbovirus co-infection in suspected febrile malaria and typhoid patients in Nigeria. J Infect Dev Ctries, 2013; 7:51-9.
28. Ochiai RL, Acosta CJ, Danovaro-Holliday MC, Baiqing D, Bhattacharya SK, Agtini MD, *et al*. A study of typhoid fever in five Asian countries: disease burden and implications for controls. Bull World Health Organ, 2008; 86:260-268.
29. WHO SEARO. Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic Fever Revised and expanded, 2011. Available at: http://www.searo.who.int/entity/vector_borne_tropical_ diseas es/documents/en. Accessed on 15/04/2014.
30. Lee IK, Liu JW, Yang KD. Clinical characteristics and risk factors for concurrent bacteremia in adults with dengue hemorrhagic fever. Am J Trop Med Hyg, 2005; 72:221-226.
31. Mathew A, Kurane I, Green S, Vaughn DW, Kalayanarooj S, Suntayakorn S, *et al*. Impaired T cell proliferation in acute dengue infection. J Immunol, 1999; 162:5609-5615.
32. See KC, Phua J, Yip HS, Yeo LL, Lim TK. Identification of concurrent bacterial infection in adult patients with dengue. Am J Trop Med Hyg, 2013; 89:804-810.