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Evaluation of serum parameters in children of age less than 10 years diagnosed with dengue fever

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Abstract
Dengue fever is an acute febrile disease, endemic in tropics, caused by four closely related Dengue viruses. It is transmitted to humans by the Aedes aegypti mosquito, which unlike the malaria causing mosquito Anopheles feeds only during the day. The disease is now spreading internationally. Dengue is not contagious. It spreads only through the bite of an infected mosquito. Dengue presents with sudden onset of fever, severe headache, muscle and joint pains (severe pain that gives it the nick-name break-bone fever) and rashes on the body. There may also be gastritis with abdominal pain, nausea, vomiting, or diarrhoea. Hence based on above findings the present study was planned for Evaluation of Serum Parameters in Children of Age Less than 10 years Diagnosed with Dengue Fever.
The comprehensive study was conducted for the duration of 1 year (2018-2019) in the Upgraded Department of Paediatrics, Patna Medical College & Hospital, Patna, Bihar, India. Total 755 children below age of 10 years referred to our department were enrolled in the present study. Out of that 30 cases were found positive for the dengue fever.
Hospital based studies on the risk of shock and death in severe dengue in tropical Asian countries showed that the percentage of admitted cases developing shock, ranged from 9 to 60% and within hospital, case fatality rates ranging from 0.2 to over 9%. Early recognition and prompt initiation of appropriate treatment are vital to reduce disease related morbidity and mortality. Focus should be on effective implementation of surveillance, vector control measures through source reduction and personal prophylaxis against mosquito bites, especially during monsoon months.

Keywords: Dengue, acute febrile, endemic in tropics, serum

1. Introduction
Dengue is the most common and important arthropod-borne viral (arboviral) illness in humans. It is transmitted by mosquitoes of the genus Aedes, which are widely distributed in subtropical and tropical areas of the world. The incidence of dengue has increased dramatically in recent decades, with estimates of 40%-50% of the world's population are at risk for the disease in tropical, subtropical and most recently, more temperate areas [1].
A small percentage of person who have previously been infected by one dengue serotype develop bleeding and endothelial leak upon infection with another dengue serotype. This syndrome is termed severe dengue (also known as dengue hemorrhagic fever and dengue shock syndrome). Dengue fever is typically a self-limited disease with a mortality rate of less than 1% when detected early and with access to proper medical care. When treated, severe dengue has a mortality rate of 2%-5%, but, when left untreated, the mortality rate is as high as 20%. On average, dengue becomes symptomatic after a 4- to 10-day incubation period (range, 3-14 days). Dengue symptoms usually lasts for 2-7 days.
Many individuals with dengue may be asymptomatic. Many patients with dengue experience a prodrome of chills, rashes, including erythematous mottling of the skin and facial flushing which may last 2-3 days. Children younger than 15 years who have dengue usually have a nonspecific febrile syndrome, which may be accompanied by a maculopapular rash. Dengue should be suspected in individuals who present with high fever (104°F/40°C), retro-orbital headache, muscle and joint pain, nausea, vomiting, and rashes and who have travelled within 2 weeks of symptom onset to an area where appropriate vectors are present and dengue transmission may be occurring.
The initial phase of severe dengue is similar to that of dengue fever and other febrile viral illnesses. Shortly after the fever breaks (3-7 days after symptom onset or sometimes within 24 hours before), signs of plasma leakage appear, along with the development of hemorrhagic symptoms such as bleeding from sites of trauma, gastrointestinal bleeding, epistaxis and hematuria. Patients may also present with severe abdominal pain, persistent vomiting that may contain blood, fatigue, and febrile seizures (in children).
The subsequent 24 hours frequently prove critical. If left untreated, hemorrhagic fever most likely progresses to shock. Common symptoms in impending shock include abdominal pain, vomiting, and restlessness. Patients also may have symptoms related to circulatory failure, such as pallor, tachypnea, tachycardia, dizziness and a decreased level of consciousness.
Globally, 2.5-3 billion individuals live in approximately 112 countries that experience dengue transmission. While the annual incidence is unclear owing to incomplete global reporting and misclassification of illness, approximately 3.2 million individuals were infected globally in 2015. It is caused by infection with 1 of the 4 serotypes of dengue virus, which is a Flavivirus (a genus of single-stranded

nonsegmented RNA viruses). Infection with one dengue serotype confers lifelong homotypic immunity to that serotype and a brief period (approximately 2 years) of partial heterotypic immunity to other serotypes, but an individual can eventually be infected by all 4 serotypes. Several serotypes can be in circulation during an epidemic.

Dengue is transmitted by mosquitoes of the genus Aedes, which are widely distributed in subtropical and tropical areas of the world. An individual with dengue is capable of transmitting the virus for 4-5 days (maximum 12 days) to a capable vector. After an incubation period of 4-10 days, the infected mosquito can transmit virus for the rest of its life span (2 weeks to 1 month). Aedes albopictus is more cold tolerant than Aedes aegypti, so it can survive and transmit virus in the more temperate regions of the United States and Europe.

The global incidence of dengue has increased dramatically in the last several decades, with an estimated 40%-50% of the world's population in 128 countries at risk [2, 3, 4]. Today, severe dengue largely affects Asian and Latin American countries, where it is the leading cause of hospitalization and death. The World Health Organization (WHO) ranked dengue as one of the top ten threats to global health in 2019 [5].

Initial dengue infection may be asymptomatic (50%-90%) [6], may result in a nonspecific febrile illness, or may produce the symptom complex of classic dengue fever (DF). Classic dengue fever is marked by rapid onset of high fever, headache, retro-orbital pain, diffuse body pain (both muscle and bone), weakness, vomiting, sore throat, altered taste sensation, and a centrifugal maculopapular rash, among other manifestations. The severity of the pain led to the term break bone fever to describe dengue.

A small percentage of persons who have previously been infected by one dengue serotype develop bleeding and endothelial leak upon infection with another dengue serotype. This syndrome is termed severe dengue (reclassified in 2009 by the WHO, previously referred to as dengue hemo rrhagic fever and dengue shock syndrome).

Severe dengue has also been termed dengue vasculopathy. Vascular leakage in these patients results in hemo concentration and serous effusions and can lead to circulatory collapse. This, in conjunction with severe hemorrhagic complications, can lead to a shock syndrome, which poses a greater fatality risk than bleeding per se [7].

Dengue virus transmission follows 2 general patterns: epidemic dengue and hyper endemic dengue. Epidemic dengue transmission occurs when dengue virus is introduced into a region as an isolated event that involves a single viral strain. If the number of vectors and susceptible paediatric and adult hosts is sufficient, explosive transmission can occur, with an infection incidence of 25-50%. Mosquito-control efforts, changes in weather and herd immunity contribute to the control of these epidemics. Transmission appears to begin in urban centres and then spreads to the rest of the country [8]. This is the current pattern of transmission in parts of Africa and South America, areas of Asia where the virus has re-emerged and small island nations. Travellers to these areas are at increased risk of acquiring dengue during these periods of epidemic transmission.

Hyper endemic dengue transmission is characterized by the continuous circulation of multiple viral serotypes in an area where a large pool of susceptible hosts and a competent vector (with or without seasonal variation) are constantly present. This is the predominant pattern of global transmission. In areas of hyper endemic dengue, antibody prevalence increases with age and most adults are immune. Hyper endemic transmission appears to be a major risk for dengue hemorrhagic fever. Travellers to these areas are more likely to be infected than are travellers to areas that experience only epidemic transmission [9].

Because the signs and symptoms of dengue fever are nonspecific, attempting laboratory confirmation of dengue infection by serodiagnosis, reverse-transcriptase polymerase chain reaction (RT-PCR) or culture is important. Serodiagnosis is made on the basis of a rise in antibody titre in paired IgG or IgM specimens. Results vary depending on whether the infection is primary or secondary (see Presentation and Workup). Dengue is a reportable disease in the United States, known or suspected cases should be reported to public health authorities.

Dengue fever is usually a self-limited illness. Supportive care with analgesics, judicious fluid replacement, and bed rest is usually sufficient. Successful management of severe dengue requires intravascular volume replacement with careful attention to fluid management and proactive treatment of hemorrhage. Admission to an intensive care unit is indicated for patients with severe dengue.

The earliest known documentation of dengue fever–like illness was in the Chinese Encyclopaedia of Symptoms during the Chin Dynasty (CE 265-420). The illness was called "the water poison" and was associated with flying insects near water. Outbreaks of febrile illnesses compatible with dengue fever have been recorded throughout history, with the first epidemic described in 1635 in the West Indies.

In 1779-1780, the first confirmed reported outbreak of dengue fever occurred almost simultaneously in Asia, North America and Africa. In 1789, the American physician Benjamin Rush published an account of a probable dengue fever epidemic that had occurred in Philadelphia in 1780. Rush coined the term break bone fever to describe the intense symptoms reported by one of his patients.

A dengue like epidemic in East Africa in the early 1820s was called, in Swahili, ki denga pepo ("it is a sudden overtaking by a spirit"). The English version of this term "Dandy fever" was applied to an 1827-28 Caribbean outbreak and in the Spanish Caribbean colonies, that term was altered to "dengue."

Probable outbreaks of dengue fever occurred sporadically every 10-30 years until after World War II. The socioeconomic disruptions caused by World War II resulted in increased worldwide spread of dengue viruses and capable vectors. The first epidemic of dengue hemo rrhagic fever in the modern era was described in Manila in 1953. After that, outbreaks of dengue fever became more common.

A pattern developed in which dengue fever epidemics occurred with increasing frequency and were associated with occasional dengue hemo rrhagic fever cases. Subsequently, dengue hemo rrhagic fever epidemics occurred every few years. Eventually, dengue hemo rrhagic fever epidemics occurred yearly, with major outbreaks occurring approximately every 3 years. This pattern has repeated itself as dengue fever has spread to new regions.

Although initial epidemics were located in urban areas, increased dengue spread has involved suburban and rural locals in Asia and Latin America. The only continents that do not experience dengue transmission are Europe and

Antarctica. In the 1950s, 9 countries reported dengue outbreaks, currently, the geographic distribution includes more than 100 countries worldwide. Several of these countries had not previously reported dengue and many had not reported dengue in 20 years.

Dengue transmission spread from Southeast Asia into surrounding subtropical and tropical Asian countries, southern China and southern Taiwan, the Indian subcontinent and Sri Lanka and down the island nations of Malaysia, the Philippines, New Guinea, north eastern Australia, and several Pacific islands including Tahiti, Palau, Tonga and the Cook Islands. Hyper endemic transmission is reported in Vietnam, Thailand, Indonesia, Pakistan, India, Malaysia and the Philippines. Dengue continues to extend its range.

In the Americas, dengue epidemics were rare post war because Aedes mosquitoes had been eradicated from most of the region through coordinated vector-control efforts. Systematic spraying was halted in the early 1970s because of environmental concerns. By the 1990s, A. aegypti mosquitoes repopulated most of the countries in which they had been eliminated.

In 2014, increased cases of dengue were reported to the WHO in the Peoples Republic of China, Cook Island, Fiji, Malaysia and Vanuatu which experienced an outbreak of dengue serotype 3 (DENV-3) after a 10-year hiatus. In 2015, large outbreaks of dengue were reported in the Philippines (>169,000 cases), Malaysia (>111,000 suspected cases), and Brazil (>1.5 million cases). Delhi, India, experienced its worse outbreak since 2006.

The period to be really watchful in dengue is after the first 2-4 days called the critical phase as the fever reduces. That is when shock develops. Shock occurs as the fluid portion of the blood (plasma) leaks into the abdomen, lung spaces etc. This fluid leak apart from causing shock can cause abdominal distension and respiratory problems. Bleeding can also occur if the shock is undetected or not treated appropriately. Low platelet count per se does not cause bleeding.

Like most viral infections there is no specific treatment for Dengue, only simple supportive care with fluids. No antibiotics are needed to treat this viral infection. Bring the temperature down. A very high temperature can be dangerous and can cause fits in young children known as febrile convulsions. To bring down high fever to below 39 deg C, gently sponge the child with cloth soaked in water and give paracetamol. Avoid certain drugs, for example, aspirin, NSAIDs (not steroidal inflammatory drugs such as ibuprofen) which can worsen platelet problems and also cause gastritis leading to bleeds.The mainstay of treatment is timely supportive therapy with fluids, oral or intravenous route. Shock can be detected clinically by the degree of rise in hematocrit as the fluid leaks into body spaces. Increased oral fluid intake is recommended. Always use oral fluids if one is able to drink. Supplementation with intravenous fluids may be necessary if the patient is unable to maintain oral intake and / or is in shock. Close monitoring in this critical period is crucial. Blood products will be needed only if the patient is bleeding, usual site of bleed is the gut. The platelet count is the last to recover. Doctors are not unduly concerned by the low platelet count and platelet transfusions are not needed for just a low platelet count if there is no bleeding. Hence based on above findings the present study Was planned for Evaluation of Serum Parameters in Children of Age Less than 10 years Diagnosed with Dengue Fever.

Methodology

The comprehensive study was conducted for the duration of 1 year (2018-2019) in the Upgraded Department of Paediatrics, Patna Medical College & Hospital, Patna, Bihar, India. Total 755 children below age of 10 years referred to our department were enrolled in the present study. Out of that 30 cases were found positive for the dengue fever.

A detailed history of each case was recorded in pre-structured case record forms including symptoms, signs and laboratory investigations. Detailed clinical examination was done at the time of admission and close follow up of the child was done to watch for progression of disease. Blood pressure was measured by using an appropriate age matched cuff. Tourniquet test was done in those children who did not have obvious bleeding manifestations.

Informed consents were taken from the parents of all patients. The aims and the objectives of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to the conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion criteria

Age group of 0 to 10 years, both genders, patients with NS1 Ag positive, serologically confirmed IgM positive dengue fever.

Exclusion criteria

Age group >10 years, preexisting chronic diseases.

Results and Discussion

An estimated 50 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries [8]. In India, there is increased proportion of Dengue cases with severe disease. The dengue epidemics in India are cyclical and are more frequent, expanding geographically into the rural areas and all forms of serotypes are circulating in the community [9]. Uncontrolled population growth, urbanization, inadequate waste water management and lack of effective mosquito control have been implicated in the increased distribution and density of the vector and also the increased spread of the virus [10]. The manifestation of dengue fever vary from asymptomatic to severe dengue fever and differ from epidemic to epidemic with atypical manifestation. Early recognition of severe dengue infection and proper treatment is very important to reduce the morbidity and mortality. WHO revised their guidelines in 2009 [11] and accordingly the clinical classification was revised as dengue without warning signs, dengue with warning signs, and severe dengue which was more appropriate and much easier to understand. [12]. It also helped in identifying sick dengue patients easier for the clinicians than the traditional guidelines [13]. The warning signs in the revised classification were put forth to identify the severe dengue cases by health care professionals early during endemic and facilitated them for the need of admission and more intensive monitoring without the help of detailed laboratory workup [12-13].

Table 1: Demographic details

Demographic data	No. of Cases
Positive Cases	30
Males	19
Females	11
Age (years)	
1 – 2 years	5
2 – 4 years	6
4 – 6 years	4
6 – 8 years	7
8 – 10 years	8
Locality	
Urban	21
Rural	9

Table 2: Distribution of dengue cases as per revised WHO criteria

Classification	Number of cases
Dengue without warning signs	6
Dengue with warning signs	19
Severe dengue	5
Total	30

Table 3: Clinical manifestation according to type of dengue fever cases.

Symptoms and sign	Number of cases
Fever	24
Myalgia	22
Headache	16
Cough	5
Abdominal pain	4
Rashes	4
Epistaxis	2
Hepato splenomegaly	3
Gum bleeding	2
Hematuria	2
Vomiting	12
Retro-orbital pain	5

Table 4: Laboratory parameters in dengue fever cases.

Criteria	No. of cases
Raised hematocrit >35%	16
Leucopenia <5000	13
Thrombocytopenia <1.5 lakh/cu mm	21
Thrombocytopenia <1 lakh/cu mm	18
Thrombocytopenia <50000/cu mm	5
Serum bilirubin>2 mg/dl	6
Serum creatinine >1.5 mg/dl	4

Male preponderance among dengue cases has also been reported in previous studies [15]. Low prevalence among females may be due to low reporting rate and indoor/household activities, using covered clothes may be another cause for less exposure to risk of vector borne infection [14]. Significant numbers of cases were reported from urban areas. Dengue is a disease of urban areas where solid wastes, air conditioners, air coolers, flower pots and so forth are the major contributors in the growth of the vector [16]. Increased positivity is due to the favourable temperature and humidity condition which helps mosquitoes to breed [17-20]. The presence of stagnant water after rainfall favours breeding of the mosquito vector, results in large number of dengue cases. As the monsoon season favours breeding of Aedes mosquitoes, effective preventive and control measures to be taken prior to and with the beginning of monsoon to reduce the occurrence of dengue in the community [19-20]. The male to female ratio in this study was 1.8:1 respectively. Congruent pattern was also seen in the retrospective analysis of the 2006 North Indian Dengue outbreak [21].

The clinical profile of dengue revealed that fever was the most common presenting symptom. Similar studies in and around India have also substantiated fever as being the most common presenting symptom. Fever, Myalgia, & Headache were found to be present among the study population. It is imperative to keep in mind that other infections that cause fever and gastrointestinal symptoms such as typhoid, leptospirosis, enter viral infections are common in India and may often lead to a delay in the diagnosis of dengue. Our study suggests that dengue in all its forms should be included in the differential diagnosis of patients with fever and gastrointestinal symptoms. This conclusion was also made from a study done in a tertiary care centre in Pakistan [23].

In spite of the fact that diseases of nonhuman primates do happen, viremic people are the most critical supply for dengue infections. After vector-borne transmission, the infection at first taints macrophages and dendritic cells. At that point, it recreates in provincial lymph hubs. Contamination with the infection is trailed by a brooding time of 4 to 10 days, amid which the infection moves toward becoming dispersed by means of blood and lymphatic vessels, in this manner bringing on systemic ailment. By far most of patients with dengue disease is either asymptomatic or indicates just mellow side effects [24]. If dengue diseases end up noticeably symptomatic, 3 phases can be recognized: First, a febrile stage; second, a basic stage amid defer vescence; and third, a recuperation arrange. The starting febrile stage starts with fast onset, high grade fever, which is joined by retro-orbital cerebral pain, serious myalgia and arthralgia ("break-bone fever "), nausea, vomiting (more typical in youngsters) and general exhaustion. A blended maculopapular rash, more regular in young sters shows up amid the finish of the febrile stage [25]. Dengue disease can be analysed specifically through discovery of infection parts or else in a roundabout way through serological techniques. The sort of analytic test utilized relies on the phase of the malady. Due to the intense onset and seriousness of the side effects, patients with dengue typically display inside the initial 2 days of ailment at social insurance offices. At this organize, finding just can be built up by direct popular location tests. Be that as it may, once hemo rrhagic fever or dengue stun disorder has created, determination can as it were be set up by serology on the grounds that the viremic stage is over [26]. The present study highlights the importance of dengue fever to clinicians in the areas of epidemiology, manifestations, complications and outcome of the disease. The study has the limitations inherent to a hospital record-based study, so meteorological and entomological data, information, education and communication (IEC) strategies and vector control measures initiated by the government are not correlated.

Conclusion

Hospital based studies on the risk of shock and death in severe dengue in tropical Asian countries showed that the percentage of admitted cases developing shock, ranged from 9 to 60% and with in-hospital, case fatality rates ranging from 0.2 to over 9%. Early recognition and prompt initiation

of appropriate treatment are vital to reduce disease related morbidity and mortality. Focus should be on effective implementation of surveillance, vector control measures through source reduction and personal prophylaxis against mosquito bites, especially during monsoon months.

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