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Evaluation of dengue fever with in Children's in ANMMCH with clinical & laboratory evaluation

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Abstract
Dengue has recently become a major public health problem causing significant morbidity, mortality and economic loss. Dengue is endemic in more than 100 countries. Worldwide around 2.5 billion people live in dengue prone regions and about 100 million new cases are detected each year. The WHO 2009 classification divides dengue fever into two groups: uncomplicated and severe; though the 1997 WHO classification is still widely used, classifying dengue in to 3 groups: dengue fever (DF), dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS). Hence present study was planned to evaluation of dengue fever with in childrens admitted to ANMMCH with clinical & laboratory evaluation.
The study was conducted in Department of Paediatrics, ANMMCH, Gaya, Bihar from Jan 2018 to Sept 2018. Total 50 cases of the childrens diagnosed with dengue were enrolled in the present study. Detailed history and careful clinical examination was performed on each patient. Laboratory investigations done were hemoglobin, total and differential leucocyte counts, platelet count, haematocrit, liver function tests, blood urea and serum creatinine, chest radiograph and ultrasound scan of abdomen. Blood counts were monitored periodically as and when required till resolution. Other differential diagnosis was excluded by appropriate tests. The patients were classified according to revised WHO guideline and managed appropriately.
Fever, myalgia and headache were most common symptom and hepatomegaly was most common finding in cases. Dengue is an important cause of mortality and morbidity. It presents with varied clinical manifestations. In view of the increasing burden of dengue on the public health-care system one should have a high index of suspicion. Early diagnosis and prompt intervention may help in reducing the mortality and morbidity.

Keywords: clinical & laboratory evaluation, dengue, etc

1. Introduction
Dengue fever is a mosquito-borne tropical disease caused by the dengue virus. Symptoms typically begin three to fourteen days after infection. This 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 its 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 110 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. 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) [24] 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].

The diagnosis of dengue is typically made clinically, on the basis of reported symptoms and physical examination; this applies especially in endemic areas. However, early disease can be difficult to differentiate from other viral infections. A probable diagnosis is based on the findings of fever plus two of the following: nausea and vomiting, rash, generalized pains, low white blood cell count, positive tourniquet test, or any warning sign in someone who lives in an endemic area. Warning signs typically occur before the onset of severe dengue. The tourniquet test, which is particularly useful in settings where no laboratory investigations are readily available, involves the application of a blood pressure cuff at between the diastolic and systolic pressure for five minutes, followed by the counting of any petechial hemorrhages; a higher number makes a diagnosis of dengue more likely with the cut off being more than 10 to 20 per 1 inch2 (6.25 cm2) [7].

The diagnosis should be considered in anyone who develops a fever within two weeks of being in the tropics or subtropics. It can be difficult to distinguish dengue fever and chikungunya, a similar viral infection that shares many symptoms and occurs in similar parts of the world to dengue. Often, investigations are performed to exclude other conditions that cause similar symptoms, such as malaria, leptospirosis, viral hemorrhagic fever, typhoid fever, meningococcal disease, measles, and influenza. Zika fever also has similar symptoms as dengue [8].

The earliest change detectable on laboratory investigations is a low white blood cell count, which may then be followed by low platelets and metabolic acidosis. A moderately elevated level of aminotransferase (AST and ALT) from the liver is commonly associated with low platelets and white blood cells. In severe disease, plasma leakage results in hem concentration (as indicated by a rising hematocrit) and hypoalbuminemia. Pleural effusions or ascites can be detected by physical examination when large, but the demonstration of fluid on ultrasound may assist in the early identification of dengue shock syndrome. The use of ultrasound is limited by lack of availability in many settings. Dengue shock syndrome is present if pulse pressure drops to ≤ 20 mm Hg along with peripheral vascular collapse. Peripheral vascular collapse is determined in children via delayed capillary refill, rapid heart rate, or cold extremities. While warning signs are an important aspect for early detection of potential serious disease, the evidence for any specific clinical or laboratory marker is weak [9].

The World Health Organization's 2009 classification divides dengue fever into two groups: uncomplicated and severe. This replaces the 1997 WHO classification, which needed to be simplified as it had been found to be too restrictive, though the older classification is still widely used including by the World Health Organization's Regional Office for South-East Asia as of 2011. Severe dengue is defined as that associated with severe bleeding, severe organ dysfunction, or severe plasma leakage while all other cases are uncomplicated. The 1997 classification divided dengue into undifferentiated fever, dengue fever, and dengue hemorrhagic fever. Dengue hemorrhagic fever was subdivided further into grades I–IV. Grade I is the presence only of easy bruising or a positive tourniquet test in someone with fever, grade II is the presence of spontaneous bleeding into the skin and elsewhere, grade III is the clinical evidence of shock, and grade IV is shock so severe that blood pressure and pulse cannot be detected. Grades III and IV are referred to as "dengue shock syndrome" [10].

There are no specific antiviral drugs for dengue; however, maintaining proper fluid balance is important. Treatment depends on the symptoms. Those who are able to drink, are passing urine, have no "warning signs" and are otherwise healthy can be managed at home with daily follow-up and oral rehydration therapy. Those who have other health problems, have "warning signs", or cannot manage regular follow-up should be cared for in hospital. In those with severe dengue care should be provided in an area where there is access to an intensive care unit.

Intravenous hydration, if required, is typically only needed for one or two days. In children with shock due to dengue a rapid dose of 20 mL/kg is reasonable. The rate of fluid administration is then titrated to a urinary output of 0.5–1 mL/kg/h, stable vital signs and normalization of hematocrit. The smallest amount of fluid required to achieve this is recommended [5].

Invasive medical procedures such as nasogastric intubation, intramuscular injections and arterial punctures are avoided, in view of the bleeding risk. Paracetamol (acetaminophen) is used for fever and discomfort while NSAIDs such as ibuprofen and aspirin are avoided as they might aggravate the risk of bleeding. Blood transfusion is initiated early in people presenting with unstable vital signs in the face of a decreasing hematocrit, rather than waiting for the hemoglobin concentration to decrease to some predetermined "transfusion trigger" level. Packed red blood cells or whole blood are recommended, while platelets and fresh frozen plasma are usually not. There is not enough evidence to determine if corticosteroids have a positive or negative effect in dengue fever [11].

Dengue has recently become a major public health problem causing significant morbidity, mortality and economic loss. Dengue is endemic in more than 100 countries. Worldwide around 2.5 billion people live in dengue prone regions and about 100 million new cases are detected each year [12]. The WHO 2009 classification divides dengue fever into two groups: uncomplicated and severe [13]; though the 1997 WHO classification is still widely used, classifying dengue in to 3 groups: dengue fever (DF), dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) [14-15]. Hence present study was planned to evaluation of dengue fever with in childrens admitted to ANMMCH with clinical & laboratory evaluation.

Methodology

The study was conducted in Department of Paediatrics, ANMMCH, Gaya, Bihar from Jan 2018 to Sept 2018. Total 50 cases of the childrens diagnosed with dengue were enrolled in the present study.

Detailed history and careful clinical examination was performed on each patient. Laboratory investigations done were hemoglobin, total and differential leucocyte counts, platelet count, haematocrit, liver function tests, blood urea and serum creatinine, chest radiograph and ultrasound scan of abdomen. Blood counts were monitored periodically as and when required till resolution. Other differential diagnosis was excluded by appropriate tests. The patients were classified according to revised WHO guideline and managed appropriately.

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.

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

Inclusion criteria: Patients with clinical suspicion of dengue (fever, headache, retro-orbital pain, and myalgia) criteria were included in the study.

Exclusion criteria: Fever patients with other confirmed diagnosis like malaria, leptospirosis. Patients with an ide focus or any other identified specific infection were excluded during the Study.

Results & Discussion

Increase in the number of dengue cases over the past few years has been attributed to rapid unplanned urbanization with unchecked construction activities and poor sanitation facilities contributing fertile breeding areas for mosquitoes, it is also seen that increase in alertness among medical personnel following the epidemics and availability of diagnostic tools in the hospitals have contributed to the increased detection of cases [16].

Severity of dengue infection varies from influenza-like self-limiting illness to life-threatening complications like dengue hemorrhagic fever (DHF) and dengue shock syndrome. Thrombocytopenia in dengue is related to oxidative stress.

Dengue is an important emerging problem of the tropical and sub-tropical regions today. The epidemics of dengue fever have been reported in the post-monsoon season, at every 2 - 3 year intervals. Majority of the patients in our study were diagnosed in the months of August and September which was in accordance with various other studies. These findings indicate that preventive measures against dengue virus infection should come into full action during water stagnation periods after the initial bouts of rainfall and at the end of monsoon. These findings indicate that preventive measures against dengue virus infection should come into full swing during water stagnation periods after the initial bouts of rainfall and at the end of monsoon. In this study, majority of the study subjects were males.

Table 1: Demographic details

Parameters	No. of Cases
Age:	
1 – 3 years	14
4 – 7 years	13
8 – 12 years	23
Gender:	
Males	29
Females	21
Duration of Hospital Stay:	
0 – 3 days	11
4 – 6 days	34
More than 6 days	5

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

Classification	Number of cases
Dengue without warning signs	8
Dengue with warning signs	36
Severe dengue	6
Total	50

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

Clinical symptoms	No. of cases
Fever	50
Headache	45
Myalgia	42
Rash	18
Petechiae	24
Gastrointestinal bleed	5
Diarrhoea	6
Vomiting	10
Abdominal pain	12
Fast breathing	1
Itching	14
Facial puffiness	7
Decreased urine output	25
CNS manifestation	1
Bradycardia	15
Hypotension	3
Hepatomegaly	45
Splenomegaly	13
Decreased air entry	22
Ascites	22

Table 4: Laboratory parameters in dengue fever cases.

Criteria	No. of cases
Raised hematocrit >35%	24
Leucopenia <5000	21
Thrombocytopenia <1.5 lakh/cu mm	42
Thrombocytopenia <1 lakh/cu mm	27
Thrombocytopenia <50000/cu mm	7
Serum bilirubin>2 mg/dl	8
SGOT	41
SGPT	19
Serum creatinine >1.5 mg/dl	2

Fever was present in all cases followed by headache, myalgia. This observation was similar to Singh R *et al* and Jain H Similar to Singh R *et al* we also noted thrombocytopenia in almost all cases which is thought to be due to oxidative stress [17-19].

One of the most common feature of dengue is liver dysfunction which includes hepatomegaly, raised bilirubin and transaminitis [20-21]. We also observed the similar finding in our study.

Central nervous system and respiratory involvement in the form of decreased air entry and fast breathing was present in less number of cases as compared to Ratageri VH *et al*. [22]

Yacoub *et al*. noted that clinical plasma leakage, i.e., pleural effusion, ascites, and gall bladder wall edema were correlated with disease severity [23]. Even though gall bladder wall edema was known to precede the development of ascites and effusion, abdominal ultrasonography to detect such findings was not routinely performed in the febrile phase. Thrombocytopenia is an important laboratory finding and one of the diagnostic criteria for dengue infection. Severity of thrombocytopenia was correlated with plasma viral load and the extent of plasma leakage. Several previous studies noted different cut-off platelet counts to predict the development of shock [24-26].

The duration of stay of hospitalization was almost same in both severe and non-severe cases, where some studies reported duration of stay more in severe cases [27]. Fever was the most common symptom followed in order by vomiting, myalgia, abdominal pain and retro orbital pain was found less commonly. These findings are on par with many studies in India and abroad, however some of the studies reported headache as the most common symptom [28]. The most common bleeding manifestations were petechiae and rash followed by others like gum bleeding, melena, gastro intestinal bleeding, haematemesis. These bleeding manifestations are more commonly observed in cases of severe dengue fever in our study. However findings in studies of Kobilan *et al*, Mishra B *et al* reported bleeding manifestations in non-severe cases of dengue also [29-30].

Thrombocytopenia was a common feature observed in all severe and few cases of non-severe dengue fever. In our study bleeding manifestations were correlating with platelet counts, severe thrombocytopenia were seen in all cases with gastro intestinal bleed, melena and hematemesis. But study by Harris *et al*, Murge *et al* reported no significant correlation between platelet count and bleeding manifestations [31-32]. Various other factors apart from thrombocytopenia lead to bleeding manifestations, which are decreased platelet function, fibrinogen consumption, prolongation of PT/PTT, and vasculopathy [33].

Hepatomegaly was observed in majority of cases of severe dengue in our study, as reported in studies of Joshi R, Srivastava VK *et al*. [34-35]

Conclusion

Fever, myalgia and headache were most common symptom and hepatomegaly was most common finding in cases. Dengue is an important cause of mortality and morbidity. It presents with varied clinical manifestations. In view of the increasing burden of dengue on the public health-care system one should have a high index of suspicion. Early diagnosis and prompt intervention may help in reducing the mortality and morbidity.

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