ORIGINAL RESEARCH PAPER

Medicine

KEY WORDS: Dengue fever, Aedes aegypti, Bleeding

SYSTEMIC REVIEW OF DENGUE FEVER

Dr. Tushar Krishanan Saini Junior Resident, Department of Medicine, Muzaffarnagar Medical College, Muzaffarnagar

Dr. Vikki Professor, Department of Medicine, Muzaffarnagar Medical College, Muzaffarnagar

ABSTRACT

Dengue fever is a disease caused by a family of viruses transmitted by mosquitoes. Dengue virus (DENV), a member of the Flaviviridae family, is a stranded positive – sense RNA virus, causes the most widespread mosquito- borne viral infection in humans around the world today. Dengue can affect anyone but tends to be more severe in people with compromised immune systems. Dengue hemorrhagic fever is a more severe form of a viral illness. Symptoms include headache, fever, rash, and evidence of bleeding (hemorrhage) in the body. This form of dengue fever can be life-threatening and can progress to the most severe form of the illness, dengue shock syndrome. This reviews the etiology, epidemiology, diagnosis, pathophysiology, transmissions, manifestations, diagnosis, treatment, and prevention of dengue.

INTRODUCTION:

Dengue Fever is mosquito born (Aedes aegypti or Aedes albopictus) tropical disease caused by dengue virus. Dengue is caused by one of any four related stains of viruses. Ie. Dengue virus 1, 2, 3 and 4. So a person can be infected with a dengue virus as many as four times in his or her lifetime. Aedes mosquito also spread Zika, Chikungunya and other viruses every year, upto 400 million people get infected with dengue. Approximately 100 million people get sick from infection & 40000 die from severe dengue per year. A pregnant women can pass the virus to her fetus during pregnancy or around the time of birth, there has been one documented report of dengue spread through Brest milk. It is a mosquito born, single positive stranded RNA virus of the flaviviridae family, genus – Flavivirus.

Symptoms:

Which usually begin four to six days after infection and last for upto 10 days, may include sudden, high fever, sever headache, pain behind the eye balls, sever joint & muscle pain, fatigue, nausea, vomiting, skin rash and mild bleeding (such as nose bleed, bleeding from gums) symptoms worsen and can become life threatening. This is called severe dengue, dengue hemorrhage fever or dengue shock syndrome. Server dengue happens when your blood vessels become damaged and leaky, and the number of clot forming cells (Platelets) in your blood stream drops. This can lead to shock, internal bleeding, organ failure and even death may occure.

Signs: Warming signs of sever dengue fever begin the 1st day or two day after your fever goes away and may include:-

- Severe stomach pain
- Persistent vomiting
- Bleeding from gums and nose
- Blood in urine, stool or vomit
- Bleeding under the skin which look like bruising
- Difficult or rapid breathing
- Fatigue
- Irritability or restlessness
- Being very thirsty
- Pale and cold skin

Aedes aegypti (Carrier)

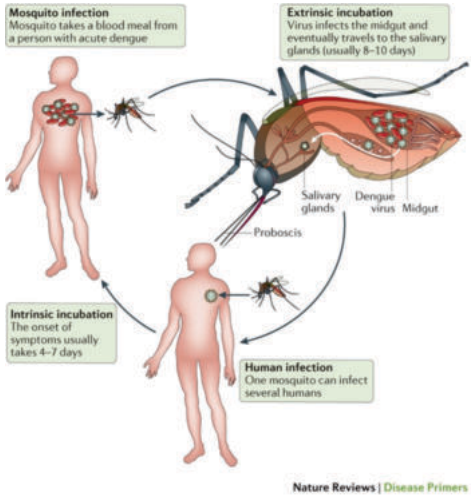
Pathophysiology:

It is characterized by the rapid onset of fever in combination with sever headache, retro- orbital pain, myalgia, arthralgia, gastro-intestinal discomfort and usually rash, minor hemorrhage manifestation may occur in form of petechial, epistaxis and gingival bleeding.

Epidemiology:

Dengue has distinct epidemiological patterns, associated with the four serotypes of the virus. These can co –circulate within a region and indeed many countries are hyper – endemic for all four serotypes. Dengue has an alarming impact on both human health and the global and national economies. More than half of the world's population is at risk of dengue infection. Each year, an estimated 390 million dengue infections occur around the world resulting in upto 3600-3700 death per year. Dengue is highly prevalent in the northern state of India, and the highest prevalence is observed in Delhi (5.6%) followed by Dadra and Nagar Haveli (3.3%) and Chandigarh (3.1%). Delhi (14.3%) and Hariyana (7.3%) Show the highest prevalence of CHICK Cases.

Mean age of dengue positive patients was 25 years (IQR 16-36), Dengue positivity was significantly higher among males. The mean monthly dengue positivity ranged from 7.7% to 37% with higher positivity reported during September and October months. The dengue serotype -2 is considered the strongest of the strain.



Causes:

Dengue fever is caused by any one of four types of dengue viruses. You cannot get dengue fever from being around an

infected person. Instead, dengue fever is spread through mosquito bites. The two type of mosquitoes that most often spread the dengue viruses are common both in and around human lodgings. When a mosquito bites a person infected with a dengue virus, the virus enters the mosquito. Than when the infected mosquito bites another person, the virus enters that person's bloodstream and causes an infection.

When you have recovered from dengue fever, you have long term immunity to the type of virus that infected you but not to the other three dengue fever virus type. This means you can infected again in the future by one of the other three virus types. Your risk of developing severe dengue fever increases if you get dengue fever a second, third or fourth time.

Risk Factors: You have a great risk of developing dengue fever or a more severe from of the diseases if:-

- You live or travel in tropical areas. Being in tropical and subtropical areas increases your risk of exposure to the virus that causes dengue fever. Especially high risk areas include Southeast Asia, the Western Pacific Islands, Latin America and Africa.
- You have had dengue fever in the past previous infection with a dengue fever virus increases your risk of severe symptoms if you get dengue fever again.
- Previous infection with DENV increases the risk of the individual developing severe dengue.
- Urbanization (especially unplanned), is associated with dengue transmission through multiple social and environmental factors-population density, human mobility, access to reliable water sources, water storage practices etc.
- Community's risk to dengue also depend on population's is knowledge, attitude and practice towards dengue, as well as the implementation of routine sustainable vector activities in the community.
- Consequently, disease risks may change and shift with climate change in tropical and subtropical areas, and vectors might adapt to new environment and climate.

Prevention and Control:
The mosquitoes that spread dengue are active during the day time.

Lover the risk of getting dengue by protecting yourself from mosquito bites by using-

- Clothes that cover as much of your body as possible
- Mosquito nets if sleeping during the day, ideally nets sprayed with insect repellent.
- Window screens.
- Mosquito repellents.
- Coils and vaporizes.

If you get dengue, it's important to:

- Rest
- Drink plenty of liquids.
- Use acetaminophen (Paracetamol) for pain.
- Avoid non-steroidal anti-inflammatory drugs like ibuprofen and asprin.
- Watch the severe symptoms and contact your doctor as soon as possible if you notice any, immediately.

Differential Diagnosis:
The clinical diagnosis of dengue can be challenging as many other illness can be present similarly, early in the disease course. Other considerations should include malaria, influenza, Zika, chikungunya, measles and yellow fever. Obtain a detailed history of immunizations, travel exposures.

Rapid laboratory identification of dengue fever includes NS1 antigen detection and serologic tests. Serological tests are only use full after several days of infection and may be associated with false positive due to other flavi virus infections. Such as yellow fever of Zika virus.

Complications:

- Liver injury
- Orchitis
- Oophoritis
- Pneumonia
- Cardiomyopathy
- Seizures
- Encephalopathy
- Encephalitis

Investigation:
Dengue NS1 Antigen
This is a blood test to detect the dengue virus early in the course of an infection.

When to get the test done: It should be done within the first five days of the appearance of symptoms because after five-seven days, the chances of false positive and negative results are high.

Limitations: This test does not differentiate between different dengue serotypes. It is also found that the sensitivity of the test is higher (more than 90%) in primary infection (first time infection) than in secondary infection.

When can you get the results: The test results can be obtained within a day. The NS1 Antigen test is comparatively cheaper than other lab tests for dengue.

Immunoglobulin M (IgM)
This test looks for IgM (antibodies) in the blood, which appear in the early course of the disease (acute infection). The test can also help to differentiate between primary (first time infection) and secondary (second time infection with any of the dengue virus) infection.

When to get the test done: It is advised to undergo a dengue antibody IgM test, if you are experiencing symptoms of dengue for more than a week or 10 days. This is because IgM levels are detectable in 50% of patients by day 3 after the onset of illness, which increases to 80% by day 5 and 99% by day 10.

Limitations: This test is not advised if you have a secondary dengue infection as IgM levels are significantly low (or even undetectable) in secondary infection.

When can you get the results: Depending upon the method used to detect the antibodies, you can get the test results within 30 minutes (IgM rapid test) or around 1-2 days (IgM ELISA) and it may vary for each lab.

Immunoglobulin G (IgG)
The test is used to detect infection in the later course of the disease because the level of IgG in the blood tends to increase slowly. Usually, the level increases six to ten days after the infection and the antibodies can remain in the blood for around 90 days or for the rest of your life.

To distinguish between primary and secondary dengue infections, IgG/IgM ratio test is commonly used.

When to get the test done: You can get an IgG antibody test for dengue after a week. You can also get the test done after 15 days as these antibodies can still be detected in the blood several months after the infection.

Limitations: This test is not advised for acute infections.

When can you get the results: To get the reports, you may have to wait for at least seven days or more?

Dengue RNA PCR test
It is a primary test used to detect dengue virus in the early

course of the infection. A positive result not only confirms the infection but also helps to identify the different serotypes of the dengue virus. The test is around 90% sensitive and 95% specific.

When to get the test done: The dengue RNA PCR test can provide positive results if the test is done within five days after the symptoms start to appear. It detects the viral genome (the genetic material of the virus) in the blood.

Limitations: The test can only be performed in certain laboratories.

When can you get the results: The results for dengue RNA PCR test can be obtained within a day or two after getting tested?

So if your doctor has advised a test for the diagnosis of dengue fever or if you are planning to undergo a test because you suspect you might have dengue, book the correct diagnostic test after monitoring the symptoms. Here are few common FAQs on dengue answered.

Nucleic Acid Amplification Tests (NAATs)
For patients with suspected dengue virus disease, NAATs are the preferred method of laboratory diagnosis. NAATs should be performed on serum specimens collected 7 days or less after symptom onset.

Key Facts:
Clinicians should consider dengue in a patient with a clinically compatible illness, and who lives in or recently traveled to a disease-endemic area in the 2 weeks before symptom onset.

Patients typically present with acute onset of fever, headache, body aches, and sometimes rash spreading from the trunk.

All patients with clinically suspected dengue should receive appropriate management to monitor for shock and reduce the risk of complications resulting from increased vascular permeability and plasma leakage and organ damage without waiting for diagnostic test results to be received.

In the United States, because dengue is a nationally notifiable disease, all suspected cases should be reported to the local health department.

Diagnostic Testing
Most state health departments and many commercial laboratories perform dengue diagnostic testing.

Nucleic acid amplification tests (NAATs)
- For patients with suspected dengue virus disease, NAATs are the preferred method of laboratory diagnosis.
- NAATs should be performed on serum specimens collected 7 days or less after symptom onset.
- Laboratory confirmation can be made from a single acute-phase serum specimen obtained early (≤7 days after fever onset) in the illness by detecting viral genomic sequences with rRT-PCR or dengue nonstructural protein 1 (NS1) antigen by immunoassay.
- Presence of virus by rRT-PCR or NS1 antigen in a single diagnostic specimen is considered laboratory confirmation of dengue in patients with a compatible clinical and travel history.

Serologic Tests
- IgM antibody testing can identify additional infections and is an important diagnostic tool. However, interpreting the results is complicated by cross-reactivity with other flaviviruses, like Zika, and determining the specific timing of infection can be difficult.
- Later in the illness (≥4 days after fever onset), IgM against dengue virus can be detected with MAC-ELISA. For patients presenting during the first week after fever onset, diagnostic testing should include a test for dengue virus (rRT-PCR or NS1) and IgM.
- For patients presenting >1 week after fever onset, IgM detection is most useful, although NS1 has been reported positive up to 12 days after fever onset (Figure 3-01). In the United States, both MAC-ELISA and rRT-PCR are approved as in vitro diagnostic tests.
- IgM in a single serum sample strongly suggests a recent dengue virus infection and should be presumed confirmatory for dengue if the infection occurred in a place where other potentially cross-reactive flaviviruses (such as Zika, West Nile, yellow fever, and Japanese encephalitis viruses) are not a risk.
- PRNTs can resolve false-positive IgM antibody results caused by non-specific reactivity, and, in some cases, can help identify the infecting virus. However, in areas with high prevalence of dengue and Zika virus neutralizing antibodies, PRNT may not confirm a significant proportion of IgM positive results. PRNT testing is available through several state health departments and CDC.

Cross-reactive Flaviviruses
If infection is likely to have occurred in a place where other potentially cross-reactive flaviviruses circulate, both molecular and serologic diagnostic testing for dengue and other flaviviruses should be performed. People infected with or vaccinated against other flaviviruses (such as yellow fever or Japanese encephalitis) may produce cross-reactive flavivirus antibodies, yielding false-positive serologic dengue diagnostic test results.

IgG Antibody Testing
IgG detection by ELISA in a single serum sample is not useful for diagnostic testing because it remains detectable for life after a dengue virus infection.

Treatment/Management:
Most cases of dengue fever can be treated at home with the pain medicine. Preventing mosquito bites is the best way to avoid dengue. There is no specific treatment for dengue fever exists. The focus is on treating pain symptoms. While recovering from dengue fever, drink plenty of fluids. Hospitalized If you have any sign and symptoms of dehydration, decreased urination, few or on tears, dry mouth or lips, lethargy or confusion and cold or clammy extremities.

If you have severe dengue fever, you may needs:-
- Supportive care in a hospital.
- Intravenous (IV) fluid and electrolyte replacement.
- Blood pressure monitoring.
- Transfusion to replace blood loss.

Acetaminophen (Paracetamol) is often use to control pain. Non-steroidal anti-inflammatory drugs like Ibuprofen and asprin are avoided as they can increase the risk of bleeding. There is a vaccine called Dengvaxia for people who have has dengue at least once & live in places where the disease is common. For people with severe dengue, hospitalization is often needed.

Treatment of dengue depends on the patient's illness phase. Those presenting early without any warning signs can be treated on an outpatient basis with acetaminophen and adequate oral fluids. Such patients should receive an explanation regarding the danger signs and be asked to report to the hospital immediately they notice any patients with warming signs, severe dengue, or other situation like infancy, elderly, pregnancy, diabetes and those living alone need to be admitted. Those with warming signs can be initiated on I.V. crystalloids and the fluid rate maintained on the patient response.

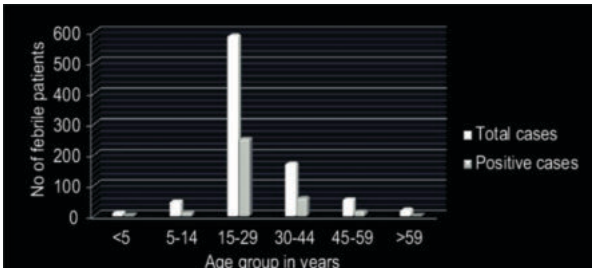
Prevention:

(a)Vaccine:-

Where dengue fever is common, one dengue fever vaccine (Dengvixia) is approved for the people age 9 to 45 who have already had dengue fever at least once. The vaccine is given in three doses over the courses of 12 months. The vaccine is approved only for "people who have a documented history of dengue fever.

Prevent Mosquito bites: preventing the mosquito bites and controlling the mosquito population are still the main methods for preventing the spread of dengue fever.

- Stay in air-conditioned or will screened housing.
- Wear protective clothing – wear a long sleeved shirt, long pants, socks & shoes.
- Use mosquito repellent.
- Reduce mosquito habitat - Lower the mesquite populations by eliminating their habitats where they lay their eggs.



A bar chart comparing the age distribution of the febrile patients and dengue positive cases.

Diagnosis:

Diagnosing dengue fever can be difficult because its sign and Symptoms can be easily confused with those of other diseases, such as Chikungunya, Zika virus, malaria and typhoid fever. Doctor will likely ask about patient's medical and travel history and any contact you may have had with mosquitoes. Collect the sample of blood to be tested in the lab for evidence of infection with one of the dengue viruses.

Prognosis:

Most people with dengue recover without any ongoing problems. Ricks of death among those with severe dengue is 0.8% to 2.5% and with adequate treatment is less that 1%. The risk of death among children less than five years old is four times greater than among those over the age of 10 year. Elderly people are also at high risk of a poor outcome.

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