DENGUE FEVER IN INDIA - A REVIEW
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Abstract
Dengue fever is generally a mosquito borne viral infection which is transmitted from female Aedes Aegypti mosquito to human or infected human to mosquito, this virus is classified into five serotypes. Presenting features may range from asymptomatic to symptomatic (High grade fever, vomiting, hemorrhage, joint pain, headache...etc.) Early and accurate diagnosis is critical to reduce mortality. Hematological tests includes RBC count, WBC count and Platelet count. We can protect ourselves from mosquito bites by using mosquito nets treated with Permethrin and getting rid of mosquito breeding sites. It is important to see a doctor when the symptoms become severe.

Keywords: Aedes Aegypti mosquito, Symptomatic, Serotypes, Mortality, Hematological test.

Introduction
Dengue fever is generally a mosquito-borne viral infection occurring all around the world in certain tropical and subtropical areas. The recurring of this viral infection in a particular individual causes severe complications and significant risks in some cases causing organ damage. It is transmitted from female Aedes Aegypti mosquito to human or infected human to mosquito. Generally, this dengue virus is classified into 5 serotypes, and one of the types affecting an individual can cause short-term immunity dysfunctions. Subsequent infection with a different type increases the risk of severe complications [1]. There are many diagnostic tests to confirm the dengue virus such as IgG, IgM, rRt-PCR, or NS. For patients presenting >1 week after fever onset, IgM detection is most useful, and NS1 has been reported positive up to 12 days after fever onset. Before 5 days of illness, dengue infection can be diagnosed by virus isolation cell culture during the febrile period. Generally, the viral RNA by nucleic acid amplification tests (NAAT) or detection of antigen ELISA. In the initial stage, CBC can be performed to know the decrease in the platelets hemoglobin and RBC count which is the main cause of dengue complications [2]. Dengue infection illness can last from 1-2 weeks and in severe cases can last up to 20 days to 1 month. Generally, there is no treatment for dengue mainly includes pain medications iron supplements, and blood transfusion if needed. The common dengue symptoms include –

- High-grade fever
- Joints pain
- Severe headache
- Nausea
- Vomiting
- Weakness
- Swollen glands
- Loss of appetite

Severe dengue infection symptoms can include –

- Pale and cold skin
- Being very thirsty
- Hematemesis
- Hematochezia
- Melena
- Hemorrhage of blood vessels
- Severe rashes.

People with severe dengue should take care and beware of recurring of the recurring infection. Even after recovering from the infection people may still have body weakness for a few days or a week. In case of body pains individual is suggested to take paracetamol for a few days.
Etiology
Generally, dengue infection is transmitted by the mode of a female Mosquito Aedes Aegypti. After feeding on a DENV-infected person, the virus replicates in the mosquito midgut before disseminating to secondary tissue, including the salivary glands this transmission is known as the virus extrinsic incubation period (EIP). This EIP takes 8-12 days when the temperature is between 25-30 degrees Celsius. Once the mosquito is infected it can carry the virus for the rest of its life. This above cycle is known as viral transmission through the mosquito bite [3].

3[In other cases, mosquitoes can be infected by biting an infected person. This can generally be someone with systemic dengue but also people who don’t show any signs of illness or any common symptoms. This transmission is known as viral transmission from humans to mosquitoes [3]. It occurs 2 days before someone shows symptoms of illness. Most of the people are infected for about 4-5 days, but infection can last up to 14 days.

Epidemiology
According to most recent data 100470 dengue cases were documented in India between January to October. Half the population is now at risk of dengue fever. Generally, there is an epidemiological trade and they include the host (the patient), the pathogen (dengue virus), and the environment. The highest number of dengue fever cases was reported and observed in Brazil followed by Peru, Bolivia, and India [4]. There are a few objectives of epidemiology -
• Identify the cause of the disease
• Determine the extent of dengue
• Study the progression of the disease
• Evaluate preventive and therapeutic measures.
• Develop public awareness and health care policies for precautionary measures.

Risk Factors
Virus strain DENV2 & DENV3. Pre-existing (previous infection) anti-dengue antibody immune enhancement is considered a key factor. Factors that can trigger dengue transmission have several reasons like - stagnant water, population, and unclean/unhygienic liquid consumption. Mostly half of the world’s population is now at risk of dengue overestimated figures i.e., 200-400 million infections occurring every year. Risks prone to dengue primarily depend on the knowledge of an individual, attitude, and practice towards dengue, and making changes in vector control activities among social communities.
Past DENV can increase the risk of developing severe dengue in individuals. Another factor includes dengue causing mosquitoes to be inactive during the night.

Pathophysiology
The pathophysiology of dengue is intricate and not completely perceived. Notwithstanding, it is accepted that the infection at first contaminates and duplicates in the cells of the liver and spleen. The infection then, at that point, spreads to different pieces of the body, including the blood, bone marrow, and lymph node [5].

The infection can create a few issues in the body, including:
Annihilation of platelets: The infection can obliterate platelets, including red platelets, white platelets, and platelets. This can prompt weakness, leukopenia, and thrombocytopenia.
Aggravation: The infection can likewise irritate the body. This can prompt side effects, for example, fever, migraine, muscle agony, and joint torment.

Vascular spillage: The infection can likewise make the veins release liquid. This can prompt a condition called narrow break disorder, which is portrayed by low circulatory strain, liquid gathering in the tissues, and shock.

Dispersed intravascular coagulation (DIC): DIC is a condition wherein the blood coagulates unusually. This can prompt draining issues and organ harm.
Immunizer subordinate improvement (ADE): This is a peculiarity where antibodies that are delivered in light of past dengue disease can make the second contamination more extreme.

Thrombotic thrombocytopenic purpura (TTP): This is an uncommon but serious intricacy of dengue that is described by the development of blood clusters and a low platelet count. TTP can be deadly on the off chance that it isn’t dealt with expeditiously.

Dengue Shock Condition (DSS): This is the most extreme type of dengue and is described by low pulse, liquid amassing in the tissues, and shock. DSS can be deadly if it isn’t dealt with quickly.

The Aedes Mosquito
Dengue infections are communicated by the nibble of a contaminated female Aedes mosquito. Both the guys and females require nectar for energy however the Females require a human blood feast as a wellspring of protein for the improvement of their eggs. These eggs can make due for a period and will incubate when presented with water. People are the favored hosts [6]. The harmless chomp, as a rule on the rear of the neck, and lower legs. Made the contamination effectively disseminated over the body and caused them tainted. Female Aedes go about as a vector for dengue in the wake of benefiting from the blood of an individual contaminated with the dengue infection, in this way, the tainted mosquitoes keep on sending dengue with each blood feast until the end of their lives.

Dengue Fever
Dengue shows comparability to other viral and bacterial ailments. Fever starts on the third day of sickness and perseveres for 5-8 days. Fever might reach 41°C. At times in youngsters, the fever changes An example is saddleback fever, which can all the more normally be found in dengue hemorrhagic fever.

6 [Leukopenia, lymphopenia, and thrombocytopenia are the clinical introductions, that are caused because of atrocities of the infection on bone marrow forerunner

[12]
cells. The dynamic viral replication and cell annihilation in the bone marrow cause bone and joint agony. 33% of patients with dengue fever might have gentle hemorrhagic side effects, including petechiae, gingival dying, and so forth [6].

Dengue Hemorrhagic Fever
Dengue hemorrhagic fever (break-bone fever) (DHF) can result from two consecutive diseases brought about by various serotypes. Transmission happens through the chomp of tainted Aedes mosquitoes. DHF is an intense febrile sickness portrayed by an abrupt beginning of fever, migraine, myalgia, retro-orbital agony, arthralgias, anorexia, GI conditions...etc [7]. The basic stage in DHF happens most often from around 24 hours before to 24 hours after the temperature decreases to typical or beneath. DHF additionally happens during essential Dengue infection (DENV) disease of newborn children brought into the world to DENV-insusceptible moms, and the normal single resistant gamble factor: is DENV-responsive IgG antibodies [7]. Having hereditary variables may likewise be pertinent and incline a few people toward DHF. The pathogenesis of DHF includes viral destructiveness factors and host reactions, aggregately bringing about strange hemostasis and expanded vascular porousness. DENGUE SHOCK Condition
Dengue Shock Conditions (DSS) are the serious appearance of DENV contamination. Early clinical appearances incorporate fever, anorexia, spewing, and facial flush, and the movement is joined by shortcomings, serious fretfulness, cold limits, facial paleness, stomach agony, augmentation and harm to the liver, and rash. In serious pathology discharging for 2-6 days after the beginning of fever. Leukocyte and platelet numbers will diminish as vascular porousness and liquid misfortune from the circulatory framework increment which brings about hypotension, and the lessening in platelet levels brings about respiratory misery, a huge drop in pulse might bring about hypovolemic shock. Passing may quickly happen if the low blood plasma level isn’t immediately checked by liquid replacement.

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Clinical Manifestations
Dengue can go from asymptomatic contamination or gentle sickness to extreme infection. An expected 1 out of 4 dengue infection contaminations are suggestive. Indicative dengue infection contamination most normally presents as a gentle to direct, vague, intense febrile sickness. Individuals can be contaminated with DENV on different occasions in their day-to-day existence as there are four dengue infections. Roughly 1 out of 20 patients with dengue infection progress to foster an extreme, perilous sickness called serious dengue.

Clinical discoveries incorporate sickness, heaving, rash, a throbbing painfulness, a positive tourniquet test, leukopenia, and cautioning signs: stomach torment or delicacy, diligent retching, clinical liquid collection, mucosal dying, dormancy, fretfulness, and liver broadening.

Extreme dengue
The dengue with any of the accompanying side effects: extreme plasma spillage prompting shock or liquid collection with respiratory trouble; serious dying or serious organ weakness, for example, raised transaminases ≥1,000 IU/L, debilitated awareness, or heart disability.

Dengue starts suddenly after a run-of-the-mill hatching time of 5-7 days, and the course follows 3 stages: febrile, basic, and gaining strength. During the febrile stage, the patient will encounter a fever that goes on for 2-7 days and can be biphasic. Different side effects during this stage can incorporate serious migraine, retro-orbital eye torment, muscle, joint, and bone torment, macular or maculopapular rash, and minor hemorrhagic indications like petechia, echymosis, purpura, epistaxis, draining gums, hematuria, or a positive tourniquet test result. The basic period of dengue starts at effervescence and normally enduring 24-48 hours. Patients with extreme plasma spillage might have pleural radiations, ascites, hypoproteinemia, or homoconcentration and may seem, by all accounts, to be well despite early indications of shock, serious hemorrhagic appearances, including hematemesis, ridiculous stool, or menorrhagia, particularly assuming that they have been in delayed shock. At last, the recovering stage starts as the body reabsorbs extravasated intravenous liquids and pleural and stomach emanations. It is crucial to look for guaranteed clinical consideration if you experience any side effects of dengue to forestall the movement to extreme dengue [25, 26, 27].

Diagnosis
➢ Hematological tests include:
➢ RBC Count
➢ WBC Count
➢ Platelet Count
➢ If the platelet count falls below 100,000 / μl it is considered a content feature of DHF
➢ Thrombocytopenia is usually observed during the period between day 3 and day 8 at the site of illness.

[13]
MAC-ELISA (IgM antibody capture enzyme-linked immunosuppressant assay)

MAC-ELISA has good sensitivity and specificity but only when used 5 or more days after the onset of fever [13-16].

**Treatment:**
Generally, there is no specific treatment for dengue infection to reduce the symptoms few OTC medications are used like Acetaminophen can help to reduce muscle pain and fever.

Few drugs are to be avoided during dengue infection like -
- Aspirin.
- Ibuprofen.
- Naproxen sodium.

If the symptoms are more recurrent then the infection needs more clinical observation and the patient should be admitted to the hospital.

Severe dengue infection is treated with the following measures –
- Supportive care in a hospital.
- Blood pressure monitoring.
- Body fluids and electrolyte balance.
- Clinical observation of liver and kidney.

Assuming somebody is associated with having dengue, it is suggested that they go through oral rehydration treatment if they are encountering moderate drying out because of high fever and heaving. Be that as it may, assuming somebody has serious dengue, isotonic liquids like Ringer lactate arrangement ought to be utilized to address intravascular volume shortcomings. Boluses of 10-20 mL/kg might be allowed for more than 20 minutes and rehashed on a case-by-case basis. Moreover, starch, dextran 40, or egg whites 5% at a portion of 10-20 mL/kg might be given, with starch being ideal because of potential excessive touchiness responses to dextran.

Patients with dengue hemorrhagic fever or dengue shock disorder might be released from the medical clinic when they meet specific measures, for example, being afebrile for 24 hours without antipyretics, having a decent craving, having a steady hematocrit level, and having no respiratory misery for something like 48 hours since recuperation from shock. If somebody has serious thrombocytopenia, current rules suggest severe bed rest and keeping away from NSAIDs or wellspring of injury.

Ivermectin, which is an expansive-range antiparasitic drug, has been displayed to hinder each of the four dengue serotypes in vitro by restraining the host atomic import proteins that were significant for atomic restriction of the dengue NS5 protein with RNA-subordinate RNA polymerase (RdRp) capability. In grown-up dengue patients, ivermectin 400 μg/kg for 2-3 days can be directed. Another medication, AT-752, which is an orally accessible guanosine nucleotide simply created by Atea Drugs, focuses on the RdRp capability of the NS5 protein.

Doxycycline, an expansive range antibiotic medication class anti-infection and antimalarial, has shown some viability as an antiviral against DENV1-4 in vitro by hindering NS2B-NS3 protease action, which brings about decreased viral section and replication. Celgosivir, an alpha-glucosidase inhibitor, has additionally shown antiviral movement when tried in vivo in mouse models of dengue contamination. Eltrombopag, a thrombopoietin receptor agonist that invigorates megakaryopoiesis, can be managed for three days in a short routine of 25 mg to essentially expand platelet recuperation and increment platelet build-up to over the lower typical cut off (LNL) (150 × 109/L) in 91% of patients on day-7 post-enlistment, contrasted with 55% in the benchmark group.

A platelet count more prominent than 50,000 cells/μL is likewise suggested. For immunization improvement, one antibody has been supported for the avoidance of dengue disease. Dengvaxia (CYD-TDV), a live recombinant tetravalent immunization by Sanofi Pasteur, has been enrolled in a few nations. The immunization is given in three dosages at age 0, 6, and a year. 2018, the CYD-TDV immunization had been endorsed for use and was being promoted in European endemic regions to people aged 9-45 years with earlier openness to the sickness. Dengue immunization was endorsed in the US by the FDA in 2019 for the counteraction of dengue sickness brought about by dengue infection serotypes 1, 2, 3, and 4 in people aged 9-16 years with research center-affirmed past dengue contamination who live in endemic regions. It is endorsed exclusively in people recently contaminated by any dengue infection serotype [8-11].

**Non-Pharmacological Treatment**
- Wearing garments that cover the body.
- Utilizing mosquito anti-agents on the body.
- Utilizing mosquito nets.
- Utilizing window and entryway screens.
- Treating setting up camp stuff or garments with bug repellent before use.
- On the off chance that conceivable, try not to be outside at daybreak, sunset, and afternoon.
- Eliminate any stale water around the home and try not to camp close to in any case water.
- Make sure that channels, plant pots, and different elements are not gathering water.
- Disposal of reproducing places for mosquito.
- Evasion of man-mosquito-infection contact.

**Preventive Measures:**
It is crucial to take preventive measures against dengue, and the most important one is to avoid mosquito bites. Mosquitoes that spread the dengue virus are active during the day, so it is important to protect yourself from mosquito bites during these times. To do this, you can wear long sleeves and pants while you are outdoors, use insect repellent containing DEET or picaridin, and apply it to exposed skin every 2 hours or more often if you are sweating or swimming. Sleeping under a mosquito net treated with permethrin and getting rid of mosquito breeding sites are also effective ways to prevent mosquito bites. Vaccination is available for dengue, but it is...
recommended only for people who are at high risk of getting dengue, such as those who live in or travel to areas where dengue is common. The symptoms of dengue are similar to many other diseases, the individual should precisely know about the dengue symptoms. If you experience any of the symptoms, such as high grade fever, headache, pain behind the eyes, muscle and joint pain, rash, nausea and vomiting, diarrhea, bleeding gums or nose, rapid breathing, or pale or cold skin, it is important to see a doctor right away. Keeping your surroundings clean and free of garbage, repairing any holes in screens on windows and doors, and using air conditioning or fans to keep mosquitoes out of your home are additional tips for preventing dengue. Stay informed about dengue outbreaks in your area, and be cautioned about the area you're about to travel about dengue circumstances there, if any then contact your doctor and take vaccination before travelling to that area [1, 2].

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