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OVERVIEW OF DENGUE FEVER SYMPTOMS, AND PREVENTION IN CHILDREN

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Abstract:

This review highlights the current understanding of dengue in children, including its clinical manifestations, diagnostic tests, management and prevention. We searched five databases (PubMed, EMBASE) to identify studies concerning dengue fever symptoms, and prevention in children published through, 2018. Dengue is accountable for considerable morbidity and death in children residing in tropical and subtropical regions and in kids visiting friends and family members living in these regions. Health problem can arise from infection with any of the 4 dengue virus serotypes and arrays from mild fever to possibly fatal dengue shock disorder. Babies with primary dengue infections whose mothers have some immunity versus dengue and youngsters that end up being infected with a 2nd dengue serotype after a preliminary primary dengue infection are at high threat for severe dengue. The widely accepted explanation for the development of severe illness is the antibody-dependent improvement design, which suggests that cross-reactive non-neutralizing antibodies increase viral infectivity. However, recent study into devices liable for the development of extreme dengue obstacle the antibody-dependent enhancement concept.

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INTRODUCTION:

Dengue has become an increasing public health issue over the past 50 years, particularly in Southeast Asia and Central and South America [1]. It has been recommended that there is additionally a substantial level of dengue transmission in Africa [2].Dengue infection comes from the family Flaviviridae, genus Flavivirus. It is a vector-borne condition transferred to human beings by Aedes mosquitos, primarily Aedes aegypti. This is a day-biting insect that preferentially eats human beings, taking several blood meals from one or a number of human hosts. They breed in containers and are carefully linked with human residences, thus transferring virus at higher rates in metropolitan settings. The geographical series of a second dengue vector, Aedes albopictus, has broadened considerably over the previous 30 years. However, this is a less effective vector and is currently not seen as a major factor to dengue transmission [4].The term 'dengue virus' describes a team of four genetically and antigenically related infections that are called serotypes (DENV-1 to DENV-4).

The vast majority of dengue situations, almost 95 percent, are youngsters much less compared to 15 years old [3].Dengue causes a spectrum of illness from mild fever to extreme disease with plasma leakage and shock. Babies and youngsters with second heterologous dengue infections are most in jeopardy for severe dengue condition. Laboratory diagnosis of dengue could be developed within five days of disease beginning by direct discovery of viral components in serum. After day 5, serologic diagnosis offers indirect proof of dengue. Presently, no reliable antiviral representatives are offered to deal with dengue infection. As a result, therapy remains supportive, with focus on close hematological monitoring, recognition of indication of serious condition and fluid-replacement therapy and/or blood transfusions when needed. Development of a dengue vaccine is considered a high public wellness top priority. A secure and effective dengue vaccine would also be necessary for travelers.
This review highlights the current understanding of dengue in children, including its clinical manifestations, diagnostic tests, management and prevention.

METHODOLOGY:

We searched five databases (PubMed, EMBASE) to identify studies concerning dengue fever symptoms, and prevention in children published through, 2018. We limited our studies to English language articles with human subjects. Furthermore, we searched references of included articles for more relevant data.

DISCUSSION:

- **Clinical manifestations of dengue disease**

The urban-adapted A. aegypti mosquito is commonly dispersed across tropical and subtropical areas. A map of the present circulation of dengue infection transmission that quantifies dengue virus transmission based upon available worldwide proof exists in Fig. 1 [2].International estimates of dengue virus infections based upon an assumed consistent yearly infection rate amongst an unrefined estimate of the population in jeopardy have produced figures of 50-100 million infections each year. This number is commonly pointed out and presently used by the World Health Organization (WHO) [1].Kids with mild dengue infection do not normally need a hospital stay and moderate or asymptomatic dengue infections are often not spotted by the public health surveillance system.

Dengue virus infection is usually inapparent [6], [7], yet could bring about a wide variety of clinical manifestations, from light high temperature to plasma leakage and the potentially deadly dengue shock syndrome [1]..The clinical indications of dengue in babies vary, with a greater regularity of plasma leakage and shock contrasted with dengue in older children [8], [9].Dengue illness was initially classified by the WHO into dengue fever, dengue hemorrhagic high temperature and dengue shock disorder [10]. Nevertheless, as dengue spread worldwide, it ended up being noticeable that this classification was not universally suitable for medical management [11].In 2009, the WHO provided a revised classification which differentiates between severe and non-severe dengue [1].Serious dengue is additionally recognized as dengue shock syndrome. Non-severe dengue consists of probable dengue, dengue without advising indications (previously dengue fever) and dengue with warning indications (formerly dengue hemorrhagic fever, Table 1). The risk of serious illness differs by age. In 114 babies, 1211 youngsters and 346 adults with laboratory-confirmed dengue in Nicaragua, extreme dengue or non-severe dengue with warning indicators happened in 64%, 55% and 36% of infants, youngsters and grownups specifically [9].

In enhancement to the difference between serious and nonsevere dengue, the WHO recognizes 3 phases in the clinical course of a dengue infection, i.e. the febrile, essential and recovery stage [1].Patients in the febrile stage typically develop fever, headache with or without retroorbital discomfort, myalgia, arthralgia, and a maculopapular to petechial rash. Although children normally struggle with high fever,

they are generally much less symptomatic than adults throughout this phase of the ailment [12].Mild hemorrhagic indications like petechiae and mucosal membrane layer blood loss (e.g. nose and gums) might be seen. This stage lasts for 3-7 days, after which most patients recoup without problems. However, in a small proportion of patients a systemic vascular leak syndrome becomes evident around the time of defervescence. This critical phase is defined by a progressive leukopenia along with a decrease in the platelet matter, hemorrhagic symptoms, pleural effusions, ascites and hypoproteinemia. Shock occurs when a critical volume of plasma is lost with leakage. Vascular leakage and shock are extra regular and a lot more serious in youngsters than in adults while hemorrhaging manifestations and body organ involvement are extra common in grownups [9], [13].

Clinically significant bleeding in the essential stage of dengue infection in youngsters usually takes place only in association with extensive and prolonged shock [14]. The modified vascular permeability reverts spontaneously to a typical degree after about 48-72 h during the recuperation phase. General health enhances, cravings returns, gastrointestinal symptoms abate, the hemodynamic standing stabilizes and diuresis follows [1]. People who have been contaminated with one dengue infection serotype (primary dengue virus infection) have longterm safety immunity versus re-infection with the exact same serotype. Nevertheless, the exact same person could be infected up to 4 times by heterologous virus serotypes. Children and grownups experiencing a secondary dengue infection have a much greater risk of creating severe dengue [15]. In prospective studies with Thai kids > 1 year of age, extreme dengue was 5-fold much more regular throughout secondary infection compared to throughout primary infection [16]. Infants born to mommies with recognized immunity to dengue virus are a special group at high danger for serious dengue and hospitalization throughout primary infection in the initial year of life [15].

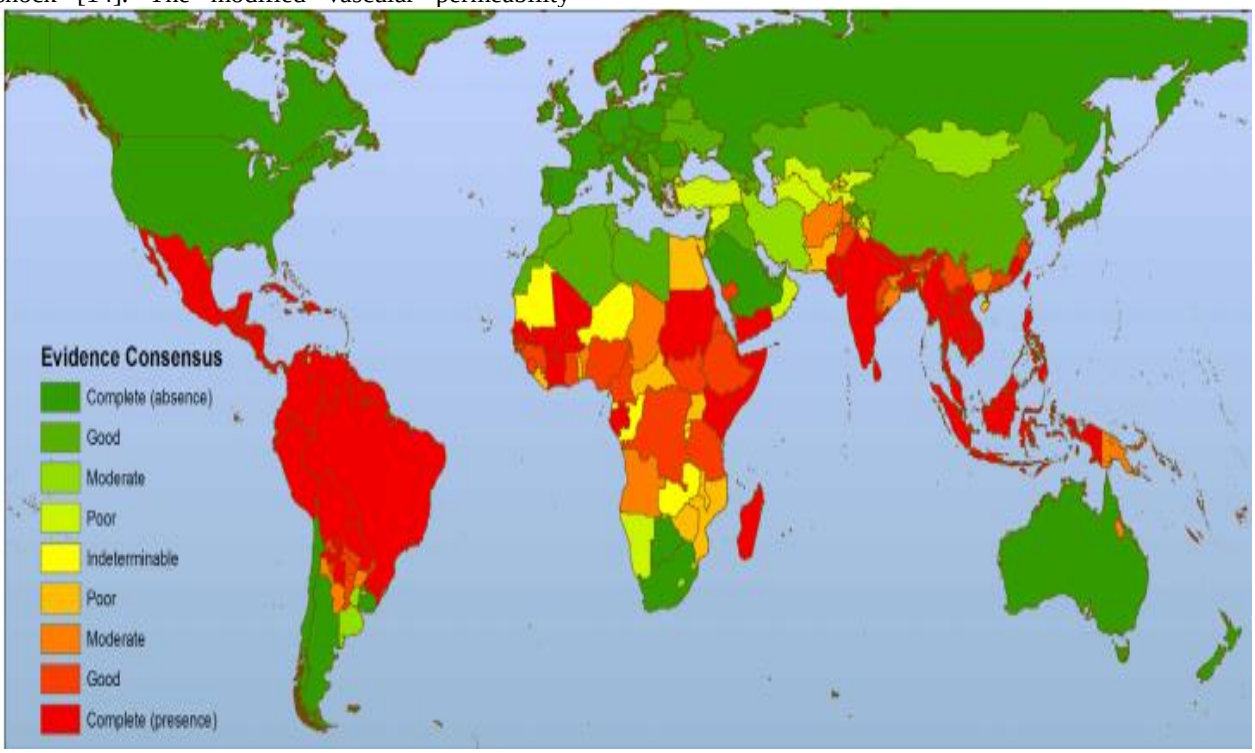

Figure 1. National and subnational evidence consensus on complete absence (green) through to complete presence (red) of dengue [2].

- **Diagnosis and management of dengue disease in children**

Diagnostic approaches to confirm dengue virus infection might entail discovery of viable virus, viral nucleic acid, peripherally circulating viral antigens or host antibodies, or a combination of these techniques. After the beginning of ailment, dengue virus can be discovered in serum, plasma, distributing blood cells and various other tissues for 4 to five days. For that reason, prior to day five of illness, dengue infections might be detected by virus isolation in cell culture, by detection of viral RNA by nucleic acid amplification examinations (e.g. reverse transcriptase-polymerase chain reaction (RTPCR)), or by discovery of viral antigens, such as the NS1 antigen, by quick tests (Fig. 2) [1].In Vietnamese babies with primary dengue infection, discovery of plasma NS1 antigen was found to be a more sensitive pen of dengue compared to real-time RT-PCR in the very first few days after illness beginning [16].This is consistent with various other descriptions of the high sensitivity of NS1 discovery in kids and adults with dengue [17], [18].A combined dengue fast test for the detection of NS1 and immunoglobulin M (IgM) or IgG antibodies had a favorable predictive value of 96% in Cambodian children who were hospitalized for an uncertainty of dengue [19].

After day 5, dengue infections and antigens go away from the blood and particular antibodies appear, making serology the approach of choice for diagnosis.1 The acquired immune action to a primary dengue infection is typically characterized by a slow and low-titer antibody rise with IgM appearing by days 3-5 and IgG obvious by days 5-7 of disease [12], [20].During an additional infection, IgM titers rise much slower than IgG titers and might lead to false negative examinations [1], [12], [20].On the other hand, IgG degrees climb quickly in recurring infection and may be found throughout the acute phase of infection. Therefore, IgM and IgG proportions may serve in distinguishing primary from secondary infection (Fig. 2) [1].Antibody discovery can be carried out using hemagglutination restraint (HI), enhance addiction, neutralization, IgM capture ELISA (MAC-ELISA), and indirect IgG ELISA assays [12], [20].A four-fold or higher increase in antibody levels gauged by IgG ELISA or by the HI test in paired sera validates acute or recent infection. However, waiting on the recovering serum gathered at the time of patient discharge is not extremely valuable for diagnosis and professional management and offers only a retrospective confirmation [1] .Cross-reaction with other flaviviruses interfere with serologic testing [20].

Although serological and molecular diagnostic tests for dengue are widely readily available, the prices, waiting time, and big instance numbers cause a scenario that case management and reporting in a lot of high worry setups is based upon clinical diagnosis alone. Dengue fever can easily be puzzled with non-dengue diseases, especially in nonepidemic situations. Depending on the geographical origin of the patient, various other etiologies ought to be eliminated. These include yellow fever, Japanese encephalitis, West Nile fever, alphaviruses (such as Sinbis and Chikungunya), malaria, leptospirosis, typhoid, measles, enteroviruses and influenza [1], [14]. Diarrhea, throwing up, petechiae, bruising, hepatomegaly and clinical proof of systemic vascular leakage, such as pleural effusion or ascites, took place a lot more frequently in babies with dengue as compared to infants with other febrile diseases in a Vietnamese potential descriptive study [16].Additionally, the median nadir in white blood cell count was substantially lower and liver transaminase levels were dramatically greater in babies with dengue as compared to babies with other febrile health problems. Additionally, a positive tourniquet test enhances the chance of dengue in youngsters providing with a febrile illness [21].Early diagnosis of dengue infection is necessary for the rapid acknowledgment of the much more severe signs and symptoms of dengue and decreases unnecessary use anti-biotics. No specific treatment for dengue is available and clinical management includes close monitoring of hematologic worth, fluid replacement therapy as required, and recognition of indicators of extreme illness (Table 1). Youngsters with potential dengue that have the ability to endure appropriate volumes of oral fluids, pass urine and do not have any of the warning signs could be sent residence with oral rehydration option and acetaminophen for high fever [1].The usage of non-steroidal anti-inflammatory representatives ought to be prevented as these medications may worsen gastritis or bleeding. A randomized controlled test in Vietnamese patients aged 5-20 years did not discover a benefit for oral prednisolone throughout the very early phase of dengue infection [22].

Kids that are sent house ought to be monitored daily by health care service providers. Children with indication and those at greater risk for serious kinds of dengue, such as infants, have to be admitted for intravenous liquid treatment and hematocrit monitoring. A double-blind randomized contrast of three different intravenous solutions in 383 Vietnamese children with moderate to extreme dengue shock disorder discovered that Ringer's

lactate (crystalloid) was as efficient in restoring cardiovascular status as either dextran or starch containing colloidal solutions. For those with refractory shock, colloidal options with starch are the safest and most reliable option for cardiovascular recovery [23].Blood transfusion with fresh-packed red cells or fresh whole blood ought to be offered as quickly as severe bleeding is presumed or acknowledged. Platelet concentrates can be given when huge blood loss could not be taken care of with fresh entire blood or fresh-packed cells [1].Finally, although steroids are assumed to stabilize capillary permeability during shock, a test of 63 kids in Thailand randomized to high-dose methylprednisolone (30 mg/kg) cannot demonstrate a benefit in early dengue shock [24].

Table 1. Diagnosis and management of dengue fever by dengue case classification. Data from World Health Organization (WHO) [1].

Diagnosis	**Diagnostic criteria**	**Management**
Probable dengue	Live in or travel to a dengue endemic area Fever and at least 2 of the following: nausea, vomiting, rash, leukopenia, arthralgia, myalgia, and a positive tourniquet test	Outpatient management with daily monitoring Oral rehydration solution Acetaminophen for treatment of fever Do not use non-steroidal anti-inflammatory agents
Dengue without warning signs (Dengue fever)	Laboratory-confirmed dengue Fever and at least 2 of the following: nausea, vomiting, rash, leukopenia, arthralgia, myalgia, and a positive tourniquet test	Hospital admission of infants, consider outpatient management with daily monitoring in children >1 year Oral rehydration solution if tolerated Closely monitor temperature pattern, fluid balance, urine output, warning signs, hematocrit, white blood cell and platelet counts
Dengue with warning signs (Dengue hemorrhagic fever)	Laboratory-confirmed dengue Fever and at least 2 of the following: nausea, vomiting, rash, leukopenia, arthralgia, myalgia, and a positive tourniquet test Any of the following warning signs: abdominal pain or tenderness, persistent emesis, volume overload (edema), mucosal bleeding, lethargy or restlessness, hepatomegaly, hemoconcentration	Intravenous crystalloid solutions Blood transfusions if necessary Monitor hematocrit, vital signs, peripheral perfusion, urine output, blood glucose and other organ functions
Severe dengue (Dengue shock syndrome)	Laboratory-confirmed dengue One of the following: shock, significant volume overload with respiratory distress, severe clinical bleeding, organ failure	Intensive care treatment Intravenous crystalloid or colloid solutions Blood transfusion with fresh-packed red cells or fresh whole blood Platelet concentrates in case of massive bleeding

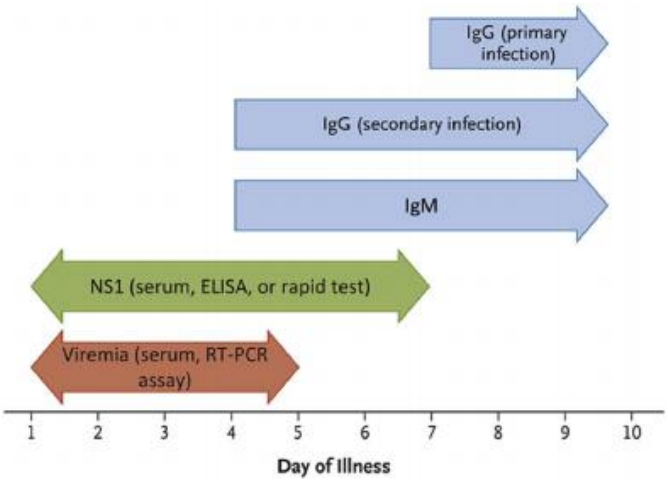

Figure 2. Laboratory diagnostic options in patients with suspected dengue infection From C.P [16].

- **Interventions for prevention and control of dengue**

Presently, vector control is the only available approach for prevention and control of dengue. Reduction of vector breeding sites with environmental clean-up campaigns to deal with disposed of or unnecessary water containers, and prevention of insect accessibility to reproducing sites is commonly promoted [1], [25].Treatment of water-storage vessels with larvicide [26] or predacious copepods [27] are used to eliminate larval stages. The performance of these treatments has been shown at a community degree, [27], [28] but hardly ever on a nationwide range, perhaps maybe in Singapore and Cuba [29], [30].Nevertheless, also when mosquito populaces have been decreased dramatically, as in Singapore, instances of dengue are still taped [29].Although space-spraying of insecticide to kill adult vectors around houses is preferred, a continual impact on virus transmission has not been demonstrated [1], [31].There is some proof that high household coverage of interior recurring spraying in an outbreak setting could decrease dengue transmission [32].The preference of Aedes vectors for daytime task and feeding means that insecticide-treated bednets are ineffective for dengue control. Numerous little trials of other insecticide-treated products, such as curtains and waterjar covers, show a decrease in indices of household vectors [33] -[35] and trials are necessitated to explore their performance on a bigger scale [35].The existence of numerous viral serotypes and the organization of previous dengue virus infection with a boosted risk for more serious condition have presented substantial obstacles to vaccine advancement. Standard live undermined vaccines (serial flow with dog kidney tissue) were provided to Thai babies and children [36], [37].Nonetheless, actions to the four serotypes after administration of these vaccines were not equivalent, bring about immunodominance which skews both the antibody and T cell actions. Live undermined chimeric injections utilizing recombinant technology have lately been developed. One such prospect vaccine, CYD-TDV, is a recombinant, live, undermined, tetravalent dengue vaccine based upon the yellow high temperature 17D vaccine pressure [38].Phase 1 and 2 tests have been taken on in children and grownups that were either immunologically natıve versus dengue and other flaviviruses before vaccination or who had some degree of pre-existing flaviviral resistance. These research studies show that a three-dose program offered over 12 months is well tolerated and elicits balanced counteracting antibody actions against the four serotypes in varied epidemiological setups [39] -[42].Recently, the results of the first scientific trial of the protective effectiveness of this investigational dengue vaccine versus virological validated dengue of any type of serotype in Thai schoolchildren were released. Efficiency estimates versus DENV1, 3 and 4 were around 70%. Conversely, efficiency was not shown against DENV2, and the truth that DENV2 was the widespread serotype during the research study, diminished the total vaccine efficiency in this study to 30.2% (95% CI 13.4-56.6). The vaccine was well tolerated without safety and security signals after 2 years of follow-up [43].Large-scale phase 3 studies in numerous epidemiological settings will give additional information for the CYDTDV vaccine.

CONCLUSION:

Dengue is accountable for considerable morbidity

and death in children residing in tropical and subtropical regions and in kids visiting friends and family members living in these regions. Health problem can arise from infection with any of the 4 dengue virus serotypes and arrays from mild fever to possibly fatal dengue shock disorder. Babies with primary dengue infections whose mothers have some immunity versus dengue and youngsters that end up being infected with a 2nd dengue serotype after a preliminary primary dengue infection are at high threat for severe dengue. The widely accepted explanation for the development of severe illness is the antibody-dependent improvement design, which suggests that cross-reactive non-neutralizing antibodies increase viral infectivity. However, recent study into devices liable for the development of extreme dengue obstacle the antibody-dependent enhancement concept.

Because of the raised number of autochthonous along with travel-associated situations, doctors around the world need to be informed with the clinical symptoms of dengue associated condition, the laboratory methods available for diagnosis, and current management recommendations. A safe and effective dengue vaccine will be the cornerstone of any kind of successful dengue control program. Up until a vaccine becomes universally available the efforts to improve treatment with application of existing best practices in triage and fluid management must continue.

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