CLINICAL PROFILE AND OUTCOME OF DENGUE FEVER AMONG CHILDREN

Dissertation submitted to

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the regulations

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M.D. BRANCH – VII

PAEDIATRICS

GOVT. STANLEY MEDICAL COLLEGE & HOSPITAL,
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CERTIFICATE

This is to certify that the dissertation entitled "**CLINICAL PROFILE AND OUTCOME OF DENGUE FEVER AMONG CHILDREN"** is the bonafide work of **Dr.S.KARTHI** in partial fulfillment of the requirements for the degree of **Doctor of Medicine in Paediatrics** Examination of the Tamilnadu Dr.M.G.R. Medical University to be held in March 2010.

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DECLARATION

I, **DR.S.KARTHI**, solemnly declare that dissertation titled, "**CLINICAL PROFILE AND OUTCOME OF DENGUE FEVER AMONG CHILDREN**" is a bonafide work done by me at The Institute of Social Paediatrics, Govt. Stanley Medical College & Hospital during 2007 – 2010 under the guidance and supervision of **DR.M.L.VASANTHAKUMARI, M.D., D.C.H.,** Director , Institute of Social Paediatrics and **DR.SUJATHA SRIDHARAN, M.D., D.C.H.,** and **DR.G.KARUNAKARAN, M.D., D.C.H.,** Professors, Institute of Social Paediatrics, Stanley Medical College, Chennai – 600 001.

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CONTENTS

INTRODUCTION

Dengue viral infections are one of the most important mosquito borne diseases in the world. They may be asymptomatic or may give rise to undifferentiated fever, dengue fever, dengue hemorrhagic fever or dengue shock syndrome. Annually, 100 million cases of dengue fever and half a million cases of DHF occur worldwide. 90 percent of DHF are children less than 15 years of age. At present, dengue is endemic in 112 countries in the world (1,2) . No vaccine is available for preventing this disease. Early recognition and prompt initiation of appropriate treatment are vital. Additional data about the disease lead to implementation or alteration in public health programs. Here, I made an attempt to study the clinical profile and outcome during July 08 to July 09.

AIM

To study the clinical profile and outcome of dengue fever in children.

SUBJECTS AND METHODS

Children less than 12 years of age with clinical features of dengue (any acute febrile illness with one of the following : myalgia, head ache ,retro-orbital pain ,bleeding ,altered sensorium, shock or low platelet count) presented at Institute of Social Pediatrics, Government Stanley Hospital, Chennai between 5th July 2008 and 10th January 2009 were registered in the study. Informed consent was obtained and detailed history was taken. For all cases ,the rapid Ig M, Ig G ELISA test was done at Government Stanley Hospital, Chennai. Children positive for Ig M alone or both Ig M and Ig G were followed up for clinical profile. Cases of enteric fever, leptospirosis, malaria were excluded by appropriate investigations. The number of children included based on the above criteria was 105. Children who were seropositive were classified on the basis of WHO criteria (2) as follows :

1. Dengue fever (DF): dengue seropositive without bleed.

2. Dengue fever with unusual bleed (DFB): dengue seropositive with bleeding tendencies, not satisfying WHO criteria for DHF.

3. Dengue hemorrhagic fever (DHF) : dengue seropositive with bleeds with evidence of plasma leakage.

4. Dengue shock syndrome (DSS): DHF with evidence of peripheral circulatory failure.

Laboratory investigations carried out in these patients included hemoglobin, blood counts, hematocrit, liver function tests etc. Chest X ray was taken to demonstrate pleural effusion. Ultra sound abdomen was done to identify ascites, polyserositis and gall bladder wall thickening. CSF analysis was done in patients with convulsions, meningeal signs and altered sensorium. Cases were managed according to the WHO protocol (2) and outcome was analyzed, using chi-square or fisher's exact test for proportions and analysis of variance for continuous data. The statistical package used was PEPI version 4.0 for windows (Abramson JH and Gahlinger PM , Sagebrush press, salt lake city). The results were compared with other studies. After analysis conclusions were arrived.

LITERATURE REVIEW

EPIDEMIOLOGY

During the 19th century, dengue was considered a sporadic disease, causing epidemics at long intervals. However, dramatic changes in this pattern have occurred and currently, dengue ranks as the most important mosquito borne viral disease in the world. In the past 50 years, its incidence has increased 30-fold with significant outbreaks occurring in five of six World Health Organization (WHO) regions. At present, dengue is endemic in 112 countries in the world(1, 2).Around 2.5 to 3 billion people, living mainly in urban areas of tropical and subtropical regions, are estimated to be at risk of acquiring dengue viral infections(2). Estimates suggest that annually 100 million cases of dengue fever and half a million cases of dengue haemorrhagic fever (DHF) occur in the world with a case fatality in Asian countries of 0.5%–3.5%(3)Of those with DHF, 90% are children less than 15 years of age(2).

Although sporadic dengue fever was known for more than 200 years, reasons for the global resurgence of epidemics of dengue fever and DHF are not very clear(4). Uncontrolled population growth, unplanned and uncontrolled urbanization, inadequate wastewater 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(4). However, microevolution of the dengue virus may have also contributed to the spread of more virulent strains around the world. In fact there is evidence that the more virulent genotypes of the virus are replacing the less virulent genotypes, which may explain the global emergence of dengue infections(2).

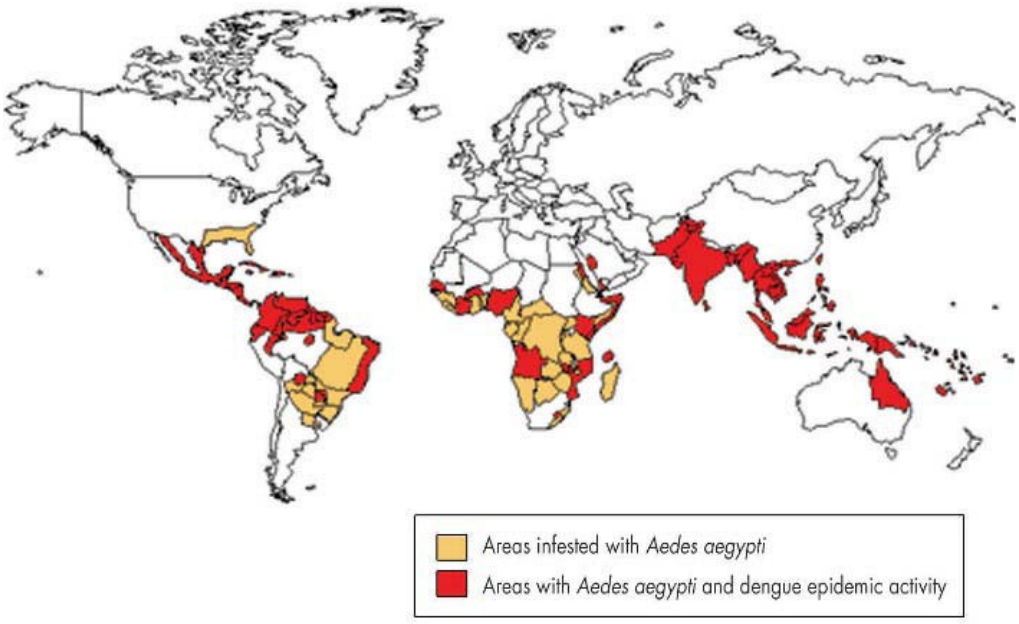
Epidemiological trends in South East Asia

The first epidemic of DHF in South East Asia occurred in 1954 in Manila, Philippines. Following this, epidemics have occurred in nearly all countries in this region, and currently are a major public health problem in seven of them. The incidence of DHF has increased dramatically in recent years with approximately five times more cases reported since 1980 than in the previous 30 years(2). Although serological surveys conducted in Indonesia showed that DEN-1 and DEN-2 were the prevalent serotypes until the late 1980s, the DEN-3 serotype has been the predominant serotype in the recent outbreaks (5).In fact, DEN-3 has been associated with severe dengue epidemics and it has been suggested that the DEN-3 virus may have certain characteristics that make it more virulent. Although DEN–4 has been isolated in almost all epidemics, it is primarily detected in secondary dengue infections (6). DHF (with an attack rate in the range 300–440cases/100 000 population) is a leading cause of hospitalization in children in South East Asia. While this rate has now fallen in Thailand (95–103 cases/100 000 population in 1997),(7)some countries such as Vietnam, still experience very high attack rates(8) Although case fatality rates in most countries in South East Asia have declined and are now less than 1%, those in some countries still exceed 4%, mainly due to late admission to hospital, when the disease is at an advanced state(9) In the newly industrialized countries such as Singapore and Malaysia, successful vector control programmes led to a gradual decline in the incidence of dengue, but even here a resurgence has been seen since 1994(9).

Epidemiological trends in South Asia

Although small outbreaks of DHF occurred South Asia between 1964 and 1966,(10) the first major epidemic of DHF occurred in Sri Lanka in 1989. Since then regular epidemics have occurred in Sri Lanka, resulting in increasing numbers of cases each year. The DEN-3 subtype III was identified as the cause of the first and subsequent epidemics in Sri Lanka along with the DEN-2 serotype(11) Dengue infections were first reported in India in 1991 (6291 cases of dengue fever), and the first epidemic of DHF occurred in Delhi in 1996(11).

Epidemiological pattern of DHF in South Asia is now similar to SEAR.



WORLD DISTRIBUTION OF PREDOMINANT DENGUE MOSQUITO VECTOR (Aedes aegypti) AND AREAS WITH DENGUE EPIDEMIC ACTIVITY.

CHARACTERISTICS OF DENGUE VIRUS:

The dengue virus is a single stranded RNA virus belonging to the flaviviridae family(4)There are four serotypes (DEN 1–4), classified according to biological and immunological criteria. The viral genome is approximately 11 kb in length(4) The mature virion consists of three structural (core, membrane associated, and envelope) and seven non-structural (NS1,NS2a, NS2b, NS3, NS4a, NS4b, and NS5) proteins. The envelope protein is involved in the main biological functions of the virus.

Non-structural proteins (NS1–NS5) expressed as both membrane associated and secreted forms have also been implicated in the pathogenesis of severe disease. Unlike other viral glycoproteins, NS1 does not form a part of the virion but gets expressed on the surface of infected cells. Preliminary evidence suggests its involvement in viral RNA replication (12).

Plasma levels of secreted NS1 (sNS1) correlate with viral titers, being higher in patients with DHF compared with dengue fever (12). Moreover, elevated free sNS1 levels within 72 hours of onset of illness identify patients at risk of developing DHF. Very high levels of NS1 protein are detected in acute phase samples from patients with secondary dengue infections but not primary infections. This suggests that NS1 may contribute to formation of circulating immune complexes, which are thought to have an important role in the pathogenesis of severe dengue infections (4).The dengue virus shares antigenic epitopes with other flaviviruses such as Japanese encephalitis virus. These shared epitopes may lead to production of cross reactive antibodies and hence interfere with serological diagnosis. However,antibodies directed to the prM protein of dengue viruses are species specific (not cross reactive with those of other flaviviruses) and may be useful for seroepidemiological studies in dengue (especially in countries where other flaviviruses are endemic)(13).

MOSQUITO VECTORS

Mosquitoes belonging to the genus aedes (Aedes aegypti, Aedes albopictus, and Aedes polynesiensis) play an important part in transmission of dengue. The primary and most important vector is A aegypti, but A albopictus and A.polynesiensis may act as vectors depending on the geographic location(2).For instance, A .albopictus has been found to sometimes transmit dengue in Thailand, Samui island, India, Singapore, and Mexico.

Aedes aegypti, a container breeding, day biting mosquito is found in tropical and subtropical areas(14). They rest indoors, mainly in living rooms and bedrooms. This maximizes man-vector contact and minimizes contact with insecticides sprayed outdoors, hence contributing to difficulty in controlling this vector(15).

Significant increases in the mosquito larval populations are seen during the rainy season. This may be a reason why epidemics of dengue tend to coincide with the rainy season(14).Furthermore, ambient temperature and relative humidity affect viral propagation in mosquitoes; rates being highest in climates resembling the rainy season(14). Environmental temperatures also affect the time to acute viraemia in female mosquitoes, being shorter with rises in temperature (15).

After biting an infected human, dengue viruses enter an adult female mosquito. The virus first replicates in the midgut, reaches the haemocoel and haemolymph, and then gains access to different tissues of the insect. After viral replication in the salivary glands, the infected mosquito can transmit the virus to another human (15). Compared with uninfected mosquitoes, infected ones take longer to complete a blood meal. This may contribute to the efficiency of A .aegypti as a dengue viral vector.

CLINICAL MANIFESTATIONS

Dengue infections may be asymptomatic or give rise to undifferentiated fever, dengue fever, dengue hemorrhagic fever or dengue shock syndrome.

DIFFERENTIAL DIAGNOSIS OF DENGUE

- Infectious mononucleosis
- Chickengunya
- Coxsackie infections
- Rickettsial infections
- Rubella
- Parvo B 19 infections
- Leptospirosis
- Influenza

DIFFERENTIAL DIAGNOSIS OF DHF

- Leptospirosis
- Chickengunya
- Kawasaki disease
- Yellow fever
- Hanta viral infections
- Meningococcal sepsis.

Undifferentiated fever

This usually follows a primary infection but may also occur during a secondary infection. Clinically it is indistinguishable from other viral infections.

Dengue fever

Dengue fever may occur either during primary or secondary infections. The onset is sudden with high fever, severe headache (especially in the retro-orbital area), arthralgia, myalgia, anorexia, abdominal discomfort, and sometimes a macular papular rash. The fever may be biphasic and tends to last for 2–7 days(16). Flushing, a characteristic feature is commonly observed on the face, neck, and chest. Coryza may also be a prominent symptom especially in infants(16).Younger children tend to present with coryza, diarrhoea, rash and seizure, and less commonly with vomiting, headache, and abdominal pain(17)

Although, haemorrhagic manifestations are uncommon in dengue fever, petechiae , pupura, gastrointestinal bleeding, epistaxis, and gingival bleeding have been observed in some individuals(18). A positive tourniquet test has been reported in many individuals with dengue fever possibly due to reduced capillary fragility (17). Recovery from dengue fever is usually uneventful, but may be prolonged especially in adults (2).

Dengue haemorrhagic fever : DHF usually follows secondary dengue infections, but may sometimes follow primary infections, especially in infants. In such infants, maternally acquired dengue antibodies are presumed to enhance primary infections (19).

The fever lasts for 2–7 days and is followed by a fall in temperature to normal or subnormal levels. At this point, the patient may recover or progress to the phase of plasma leakage. Those who remain ill despite their temperature subsiding are more likely to progress to DHF. Clinical deterioration

usually occurs during defervescence (often between days 3 and 4)(20). Tachycardia and hypotension characterize the onset of plasma leakage. When plasma leakage is severe patients may develop other signs of circulatory disturbance such as prolonged capillary refill time, narrow pulse pressures, and shock. Inadequate treatment of such patients often leads to profound shock. During the phase of plasma leakage (first 24–48 hours after onset of DHF), pleural effusions and ascites are common. Pleural effusions are usually seen on the right side; a right decubitus chest radiograph is best for detecting small effusions. Abdominal ultrasound scans may demonstrate ascites or a thickened gall bladder wall(21). Pericardial effusions may also occur. This latter complication is uncommon, but is associated with high morbidity and mortality.

In DHF, bleeding may occur from any site and does not correlate with the platelet counts. Haemorrhagic manifestations usually occur once the fever has settled(21). Minor degrees of bleeding may manifest as gum bleeding and petechiae. The commonest site of haemorrhage is the gastrointestinal tract, which manifests as haematemesis or melaena, followed by epistaxis. Vaginal bleeding is commonly reported in females(21). Convalescence in DHF is usually short and uneventful. The return of appetite is a good indicator of recovery.

Dengue shock syndrome

Dengue shock syndrome is associated with very high mortality (around 9.3%, increasing to 47% in instances of profound shock)(22). Severe plasma leakage leading to dengue shock syndrome is associated with cold blotchy skin, circumoral cyanosis, and circulatory disturbances. Acute abdominal pain and persisting vomiting are early warning signs of impeding shock. Sudden hypotension may indicate the onset of profound shock (23).Prolonged shock is often accompanied by metabolic acidosis, which may precipitate disseminated intravascular coagulation or enhance ongoing disseminated intravascular coagulation, which in turn could lead to massive haemorrhage. Dengue shock syndrome

may be accompanied by encephalopathy due to metabolic or electrolyte disturbances.

COMPLICATIONS

Severe dengue infections may give rise to many complications such as liver failure, disseminated intravascular coagulation, encephalopathy, myocarditis, acute renal failure, and haemolytic uraemic syndrome (2). Although these complications are generally rare, in recent years they have been reported with increased frequency. Whether this is a true rise or due to an increase in the total number of cases of DHF needs to be determined.

Liver failure

Since hepatocytes and Kupffer cells support viral replication, liver involvement is common in all forms of dengue infection.Its severity varies with the overall severity of the dengue infection. Levels of aspartate transaminase and alanine transaminase are significantly higher, and globulins significantly lower among patients with the more severe grades of DHF. Infection with DEN-3 or DEN-4 serotypes produce greater liver involvement (liver enzymes higher compared with infection with the other two serotypes)(39). Fulminant liver failure can occur due to hepatitis or focal necrosis of the liver causing hepatic encephalopathy and even death (40).

Encephalopathy

Encephalopathy has been reported in 0.5% of patients with DHF, and has a mortality rate of 22%. Many factors contribute towards development of encephalopathy including: hepatic dysfunction, electrolyte imbalances, cerebral oedema (caused by vascular changes leading to fluid extravasation) hypoperfusion (due to circulatory disturbances), and dengue encephalitis (41). The dengue virus has been isolated from the cerebrospinal fluid of some patients having features of encephalitis. Furthermore, in mice, breakdown of the blood-brain barrier and direct viral infection of the brain has

been shown to occur. There is suggestion that histamine might have a critical role in this process. Other neurological manifestations such as altered consciousness, seizures, spasticity of limbs, hemiplegia, and a positive Kernig's sign have also been reported in 5.4% of patients with dengue.

Myocarditis

Acute reversible myocarditis has been reported in patients with dengue infections. ST segment and T wave changes in the electrocardiogram together with low ejection fractions and global hypokinesia on radionuclide ventriculography have been found. No myocardial necrosis was detected in any of the patients. In another study, 16.7% of children had left ventricular dysfunction when assessed by two dimensional and colour Doppler echocardiography. The left ventricular failure may contribute to hypotension seen in DHF/dengue shock syndrome and may have implications in fluid management as fluid overload may worsen the condition.

PATHOGENESIS OF DENGUE FEVER/DHF

Dengue may be caused by any of the dengue viral serotypes. Generally, infection with one serotype confers future protective immunity against that particular serotype but not against other serotypes. Furthermore, when infected for a second time with a different serotype, a more severe infection may occur. This is due to a phenomenon referred to as antibody dependent enhancement, where antibodies against the first serotype enhance infection with the second serotype. However, as only 2%–4% of individuals with a secondary dengue infection develop severe disease, antibody dependent enhancement alone cannot wholly explain this process (4). At present, reasons as to why only some individuals develop symptomatic infection are not known, but active research is being pursued by several groups to clarify such mechanisms.

After the bite of an infected mosquito, the dengue virus enters the body and replicates within cells of the mononuclear phagocyte lineage (macrophages, monocytes, and Bcells). Additionally, infection of mast cells, dendritic cells, and endothelial cells are known to occur. The incubation period of dengue infections is 7–10 days. A viraemic phase follows where the patient becomes febrile and infective. Thereafter, the patient may either recover or progress to the leakage phase, leading to DHF and/or dengue shock syndrome. Peak plasma viraemia correlates with the severity of dengue infections. Differences in antibody, cytokine, and T-cell responses are seen among patients with uncomplicated dengue fever or DHF/dengue shock syndrome.

RISK FACTORS

Several risk factors have been proposed for development of DHF. These include: serotype and virulence of the infecting dengue virus, age, sex, immune status, and genetic background of the host (2,4). Case fatality and hospitalization rates due to DHF/dengue shock syndrome are highest in infants and the elderly. For instance, following a secondary DEN-2 infection, the risk of death in children is nearly 15-fold higher than that in an adult(27). DHF is also reported to be more severe among females (28).

Generally malnutrition predisposes to many infectious diseases (for example, measles or tuberculosis) and tends to correlate positively with severity of disease. However, malnutrition appears to be significantly uncommon among patients with DHF, compared with patients with other infectious diseases or healthy children(29).

DHF tends to be commoner among patients suffering from other chronic illnesses (for example, diabetes mellitus or bronchial asthma)(27,28). The DEN-2 virus is capable of replicating better within peripheral blood mononuclear cells from asthmatics than non-asthmatics. Further investigation of these different factors should help us better understand the pathogenesis of DHF and may in turn allow us to

identify possible therapeutic options.

HOST GENETIC INFLUENCES IN DENGUE VIRAL

INFECTIONS

Severe dengue infections are seen in only a minority (2%–4%) of patients with secondary dengue infections (4). Human genetic factors have been little studied in DHF, but the small proportion of antibody positive persons who develop DHF, a possible racial difference in susceptibility, and a few studies suggesting HLA associations provide support for some genetic component to variable susceptibility. For instance, in Haiti, despite hyperendemic transmission of dengue fever, DHF is not reported(30).Furthermore, in Africa, where all four dengue viral serotypes circulate and epidemics of dengue fever occur, few cases of DHF are seen(4).

LAB DIAGNOSIS OF DENGUE INFECTIONS

Virus isolation

* Mosquito cell lines.
* Mosquito inoculation technique.
* Vertebral cell culture.

Serological diagnosis

* Haemagglutination inhibition test. *ELISA.
* Complement fixation test. *
  Neutralization test. *
  Antigen capture enzyme immunosorbent assay.

Molecular diagnostic methods

* RT-PCR.

PRIMARY AND SECONDARY DENGUE

In primary dengue infections, 80% of patients demonstrate Ig M antibodies by day 5, and 99% by day 10 to 20. Ig M antibodies peak at 2 weeks and decline over the next 2 to 3 months. Ig G antibodies rise later and to lower levels as compared to Ig M, then decline gradually but persist at low levels for life.

In secondary dengue infections, there is a brisk and rapid Ig G response much higher than that seen in primary infections, which peaks at 2 weeks and then declines slowly over the next 3 to 6 months. Ig M response in secondary infections is slower and lower than Ig G with some individuals showing no detectable Ig M.

A Rough Guide for Interpretation of Dengue Serology Reports (42).

Ig M	Ig G	Interpretation
Negative	Negative	Early sample/ Not dengue
Negative	Positive(low titer)	Past dengue infection
Negative	Positive(high titer)	Secondary dengue
Positive	Negative	Primary dengue
Positive	Positive(low titer)	Current/ Recent primary dengue
Positive	Positive	Secondary dengue

Serological diagnosis

Methods used for serological diagnosis of dengue infections include: haemagglutination inhibition tests, enzyme linked immunosorbent assay (ELISA), complement fixation test and neutralization tests. Dengue specific IgM and IgG ELISA is widely used, as it is relatively inexpensive, has good sensitivity, and is quick and simple to perform(2). Most patients have measurable IgM antibodies by the fifth day of infection. On average, they become undetectable 30–60 days after the onset of illness. The sensitivity of Ig M ELISAs range from 83.9%–98.4% with a specificity of 100%(27). The range of sensitivities may be important in patients with secondary dengue where Ig M antibody titers are low (31). Antigen capture ELISAs have also been developed. The serotype of the infecting virus can also be identified using conventional or capture ELISAs (32).

The ability of dengue viruses to agglutinate goose erythrocytes is used in the haemagglutination inhibition test. A fourfold or greater rise in antibody titers is suggestive of a flavivirus infection (and not diagnostic of dengue infections).However, a single antibody titer >1/2560 is accepted as indicating

secondary dengue infection if supported by a clinical history suggestive of dengue.

Molecular detection

The sensitivity, specificity, and rapid detection of minute quantities of dengue viral material in the patient's serum makes RT-PCR useful for the detection of dengue infection early in the disease when antibodies are not detected (33). RTPCR is more sensitive than virus isolation, allows for rapid detection of dengue infections (results are usually available in 24 hours) and easier identification of the circulating serotype(33) It is useful for epidemiological studies as dengue serotypes could be identified without cross reactivity with other flavi viruses.

CASE DEFINITION (2)

The WHO has developed the following case definitions for the diagnosis of DF and DHF or DSS.

Dengue Fever

The clinical description of DF is an acute febrile illness of 2-7 days duration associated with 2 or more of the following

- Headache
- Retro orbital pain
- Myalgia /Arthralgia
- Rash
- Hemorrhagic manifestations

- Leucopenia

Suspected

Cases are classified as suspected if they are compatible with the clinical description described above.

Probable

Cases are classified as probable if they are compatible with the clinical definition and satisfy one or more of the following criteria:

- **Supportive serology** (reciprocal hemagglutination-inhibition antibody titer greater than 1280, comparable Ig G EIA titers, or positive Ig M antibody test in late acute or convalescent-phase serum specimen)
- Occurrence at the **same location and time** as other confirmed cases of DF

Confirmed

A confirmed case is one that is compatible with the clinical definition and is confirmed by the laboratory by any one of the following.

- **Isolation of Dengue virus** from serum or autopsy sample.
- Demonstration of **fourfold** or more rise in Ig G or Ig M antibody titers.
- Demonstration of virus **antigen** in serum, CSF or autopsy sample by Immunohistochemistry or ELISA.
- Detection of Dengue **virus genome** in serum, CSF or autopsy sample by PCR.

Dengue Hemorrhagic Fever:

Criteria for the diagnosis of DHF include a probable or confirmed case of dengue infection and hemorrhagic tendencies as evidenced by one or more of the following:

- A positive result from the tourniquet test
- Petechiae, ecchymoses, or purpura
- Bleeding from the mucosa, gastrointestinal tract, injection sites, or other sites
- Hematemesis or melena
- Thrombocytopenia (<100,000 cells/mm^3) and
- evidence of **plasma leakage** due to increased vascular permeability manifested by one or more of the following:
    - greater than 20% rise in average Hematocrit level for age and sex,
    - greater than 20% drop in Hematocrit level following volume replacement compared to baseline, or
    - signs of plasma leakage (e.g., pleural effusion, ascites, hypoproteinemia)

Dengue Shock Syndrome

DSS is diagnosed in cases meeting all of the above criteria plus evidence of circulatory failure, such as the following:

- Rapid, weak pulse

- Narrow pulse pressure (<20 mm Hg)
- Hypotension
- Cool, clammy skin
- Altered mental status

Grading of DHF

Grade I

FEVER + NON SPECIFIC CONSTITUTIONAL SYMPTOMS, POSITIVE TOURNIQUET TEST.

Grade II

GRADE 1 MANIFESTATIONS + SPONTANEOUS BLEEDING

Grade III

ABOVE SIGNS + CIRCULATORY FAILURE.

Grade IV

PROFOUND SHOCK.

Lab Studies

Complete blood cell count findings include the following:

- **Leukopenia**, often with lymphopenia, is observed near the end of the febrile phase of illness. Lymphocytosis, with atypical lymphocytes, commonly is seen before defervescence or shock.

- A **rise in Hematocrit greater than 20%** is a sign of hemoconcentration and precedes shock. The Hematocrit level should be monitored at least every 24 hours to facilitate early recognition of dengue hemorrhagic fever (DHF) and every 3-4 hours in severe cases of DHF or dengue shock syndrome (DSS).

- **Thrombocytopenia** has been demonstrated in up to 50% of dengue fever (DF) cases. Platelet counts of less than 100,000 are seen in DHF or DSS and occur before defervescence and the onset of shock. The platelet count should be monitored at least every 24 hours to facilitate early recognition of DHF.

- Basic metabolic panel findings include the following:

  - Hyponatremia is the most common electrolyte abnormality observed in patients with DHF or DSS.

  - Metabolic acidosis is observed in those with shock, and it must be corrected rapidly.

  - Elevated BUN is observed in those with shock.

  - Liver function test findings include the following:

  - Mild elevations in transaminase levels may be seen.

  - Low albumin is a sign of hemoconcentration.

- **Coagulation studies** may help guide therapy in patients with severe hemorrhagic manifestations. Findings are as follows:

    - Prothrombin time is prolonged.

- Activated partial thromboplastin time is prolonged.

- Low fibrinogen and elevated fibrin degradation product levels are signs of disseminated intravascular coagulation.

- Typing and **cross matching** of blood should be performed in cases of severe DHF or DSS because blood products may be required.

- Serum specimens should be sent to the laboratory for **serodiagnosis**, polymerase chain reaction (PCR), and viral isolation. Because the signs and symptoms of DF are nonspecific, attempting laboratory confirmation of dengue infection is important. Serodiagnosis is made based on a rise in antibody titer in paired immunoglobulin G (IgG) specimens or immunoglobulin M (IgM). Results vary depending on whether the infection is primary or subsequent. The IgM capture enzyme-linked immunosorbent assay (MAC-ELISA) has become the widely used assay.

Treatment of Dengue & DHF (2,39):

Febrile Phase:

In the initial phase the treatment of DF & DHF is the same and is as that of any other viral fever, i.e. symptomatic and supportive.

- Rest.

- **Paracetamo**l (not > than 4 times in 24 hrs) according to age and weight for fever above 39°C.

- **Do not** give Aspirin or Brufen. Aspirin can cause gastritis and/or bleeding. In children, Reye's syndrome (Encephalopathy) may be a serious complication.

- Do not give antibiotics as these do not help.

- **Oral Rehydration Therapy** is recommended as there may be mild to moderate Dehydration due to vomiting & high temperature.

- Food can be given as per appetite.

Dengue Hemorrhagic Fever

Patients with known or suspected DF should have their platelet count and Hematocrit measured daily from the third day of illness until 1-2 days after defervescence. Those patients with a rising hematocrit or falling platelet count should have intravascular volume deficits replaced. Those patients who improve can continue to be monitored in an outpatient setting. Those patients who do not improve should be admitted to the hospital for continued hydration.

Other **indications of Hospitalization** include:

- Patients who develop signs of Tachycardia

- ↑ CRT (> 2 sec)

- Cool and clammy extremities

- Diminished peripheral pulses

- Changes in Mental status

- Oliguria

- Sudden rise in hematocrit

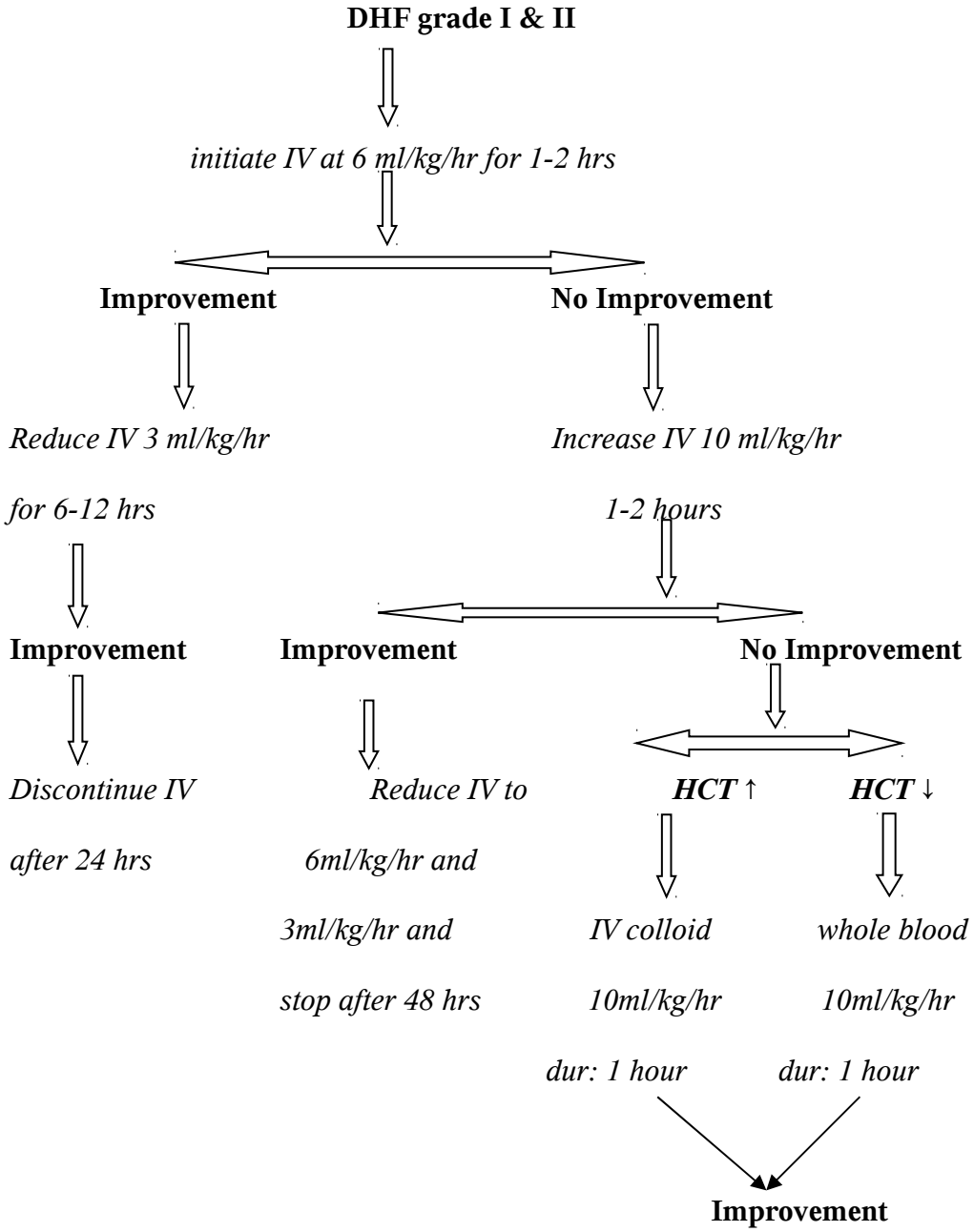
- Narrowing of pulse pressure (< 20 mm Hg)

- Hypotension (Late finding-Uncorrected shock)

Intravascular volume deficits should be corrected with isotonic fluids such as Ringer lactate solution. Boluses of 10-20 ml/kg should be given over 20 minutes and may be repeated. If this fails to correct the deficit, the hematocrit value should be determined, and, if it is rising, limited clinical information suggests that a plasma expander may be administered. Starch, dextran 40, or albumin 5% at a dose of 10-20 ml/kg may be used. If the patient does not improve after this, blood loss should be considered. Patients with internal or gastrointestinal bleeding may require transfusion. Patients with coagulopathy may require fresh frozen plasma.

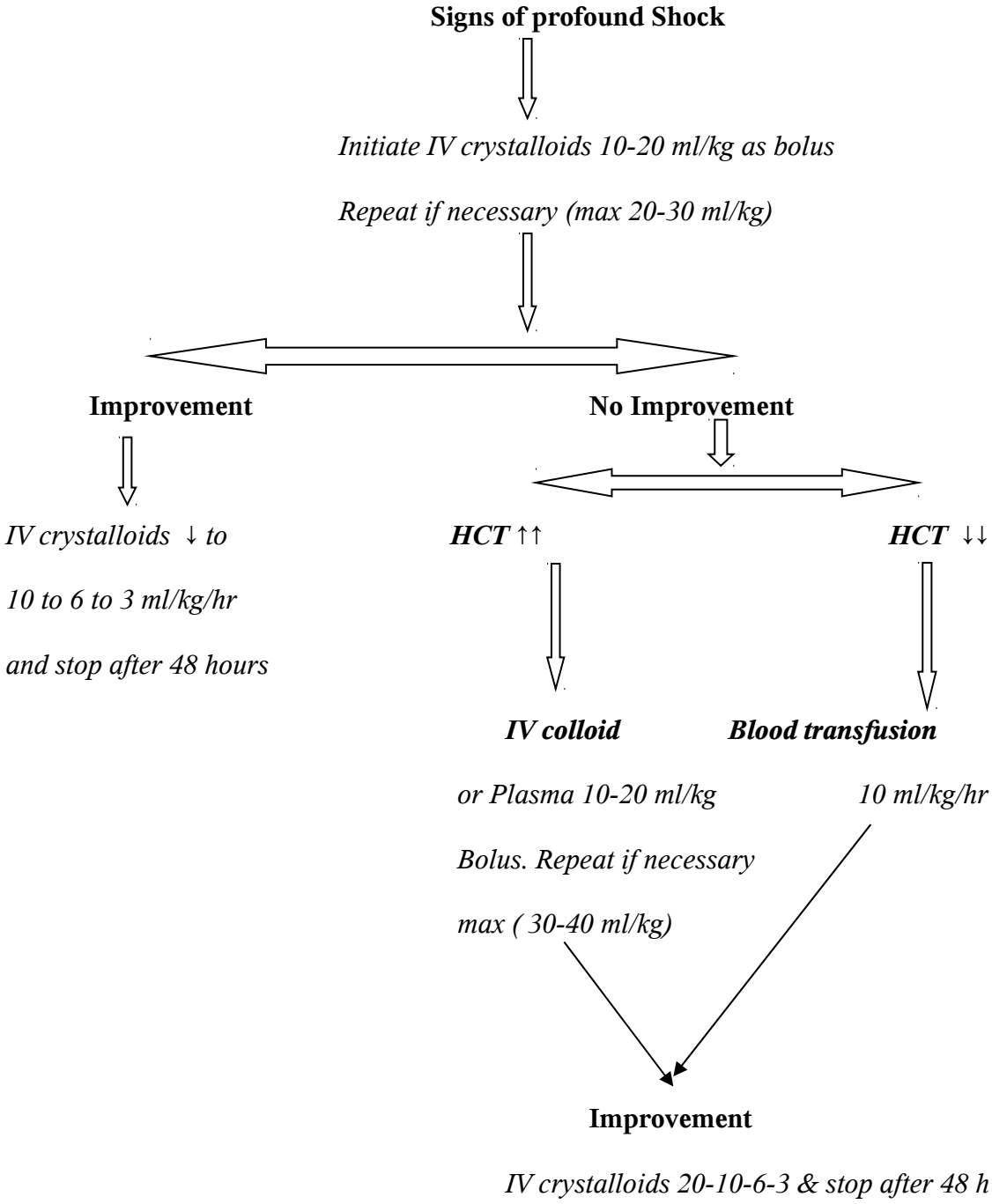
After patients with dehydration are stabilized, they usually require intravenous fluids for no more than 24-48 hours. Intravenous fluids should be stopped when the hematocrit level falls below 40% and adequate intravascular volume is present. At this time, patients reabsorb extravasated fluid and are at risk for volume overload if intravenous fluids are continued. Do not interpret a falling hematocrit value in a clinically improving patient as a sign of internal bleeding.

Fluid therapy DHF grades I and II



DHF Grade III and IV

Unstable vital signs



Fluids Recommended:

Crystalloids :

- 5% Dextrose in Isotonic NS
- 5% Dextrose in ½ NS
- 5% Dextrose in RL

- Shock Correction NS or RL

Colloids :

- Dextran 40
- Hemaccel
- Plasma

Fluid Replacement

- Volume of fluid to be just sufficient to maintain effective circulation during plasma leakage.
- Fluid charts to be made every 1 to 3 hrs and even more frequently in shock.

Change should not be drastic. e.g. don't jump from 20 ml to 6ml or vice versa. Go in a step wise manner.

Indications of Platelet / Whole blood transfusion (2)

Platelets

- Platelet count < 20,000/ cu.mm
- Platelet count >20,000 <40,000 with hemorrhagic manifestations.
- DIC

Whole Blood

- Prolonged refractory shock with ↓↓HCT even with adequate fluid replacement
- Severe massive bleeding (> 10 % of total blood volume).

Indications of FFP

(Fresh frozen Plasma)

- Plasma is used when HCT is rising despite fluid replacement
- But plasma substitutes are equally good (Dextran 40) & effective

- Essential only in cases of massive bleeding with DIC.

Monitoring of patients in DSS

- Check vitals every 15-30 minutes until shock is overcome.
- Check HCT / Platelets for every 2 hours for the first 6 hours and every 4 hours until stable.
- Fluid balance sheet to be maintained. Frequency & volume of urine output to be recorded. In refractory shock catheter may be needed.

Criteria for Discharge (2)

Patients who are resuscitated from shock recover rapidly. Patients with DHF or dengue shock syndrome (DSS) may be discharged from the hospital when they meet the following criteria:

- Afebrile for 24 hours without antipyretics
- Good appetite, clinically improved condition
- Adequate urine output
- Stable hematocrit
- At least 48 hours have passed since recovery from shock
- Absence of respiratory distress
- Platelet count greater than 50,000.

PREVENTION AND CONTROL OF DHF

Since there is no effective vaccine against dengue, the prevention and control of dengue infections depends largely on preventing man-vector contact. Numerous strategies have been adopted and include: environmental control, biological control, chemical control, and active case surveillance. While each of these methods have some effect, successful control programmes should incorporate all appropriate methods and also foster a strong partnership between the different dengue control agencies and the community. The dengue control programmes in the South East Asian and South Asian regions have been generally unsuccessful, largely because they have relied solely on insecticide spraying(2).

Environmental control methods

These include: reducing vector breeding sites, solid waste management, modification of man made breeding sites, and improvements in house design. Public education programmes play a vital part if they are to be effective (35). Personal protection is important in preventing man-vector contact. Sufficiently thick and loose fitting clothes reduce contact with the mosquitoes, but may not be the most practical clothes to wear in hot tropical climates. Other measures such as using household insecticidal products (mosquito mats and liquid vaporizers) or mosquito repellents may also be effective. Naturally occurring repellents (citronella oil, lemon grass) or chemical repellents (DEET) are available. However, unlike in the control of malaria, insecticide treated mosquito nets have limited utility in dengue as the vector is chiefly a day biting mosquito.

Biological control of vector

Biological control methods are targeted against the larval stages of the dengue vector. They include the use of larvivorous fish such as Gambusia affinis and Poecilia reticulate, endotoxin producing bacteria (Bacillus thuringiensis serotype H-14 and Bacillus sphaericus are currently used), and copepod crustaceans. Bacillus thuringiensis serotype H-14 is more effective against A aegypti with very low levels of mammalian toxicity, and has therefore been accepted for use in household containers

storing water.2 The use of mesocyclops (a copepod crustacean) in the Northern Province of Vietnam led to the eradication of the vector in a many areas(36).

Chemical control

This includes the application of larvicidal insecticides or space spraying. Space spraying is more widely used as larvicidal insecticides cost more. Insecticides used for treating containers that hold water includes Temephos 1% sand granules and insect growth regulators. Regular monitoring of resistance patterns is essential as resistance to Temephos has been reported among some aedes mosquito species in the South East Asian Region (2). Insect growth regulators interfere with the development of the immature forms of the mosquito and have extremely low mammalian toxicity. Space spraying may be applied as thermal fogs or as ultralow volume sprays. Although both methods are equally effective in killing adult mosquitoes, thermal fogging tends to be used more widely(37).

Current status of the dengue vaccine

Much research has been carried out to develop a dengue vaccine that is safe and immunogenic against all four serotypes. Although many of the vaccines developed so far (live attenuated, chimeric, DNA, and subunit vaccines) show promising results, none are sufficiently immunogenic for routine use (38).

OBSERVATIONS AND RESULTS

105 seropositive dengue cases were reported in our hospital during the study.

Dengue fever : 24 (22.8%)

Dengue fever with unusual bleeds : 32 (30.4%)

Dengue hemorrhagic fever : 29 (27.6%)

Dengue shock syndrome: 20 (19.04%)

The age group of the affected children was between 5 months to 12 years.(Mean 5.6 year, standard deviation 3.2). DSS occurred at a relatively younger age group (mean 4.04 years). But it was statistically not significant (P=0.32). Infants comprised 10.4% of total study group. 40% were children between 1 and 5 years of age. 49.5% were children between 5 and 12 years. Mean duration of fever was 5.09 days. It was 4.95, 5.25, 5.24, 4.8 days in DF, DFB, DHF, DSS respectively. Males were affected slightly more than females. It was not significant (P=0.70).

TABLE - 1

CLINICAL FEATURES

No	Feature	Total	DF	DFB	DHF	DSS	P value
1	Mean age(yr), (S.D)	5.6(3.2)	6.1(3.9)	5.7(3.1)	6.1(3.2)	4.04(3.39)	0.32
2	Male sex, no(%)	56(53)	11(45)	17(53)	18(62)	10(50)	0.70
3	Age ≤1yr, no(%)	11(10.4)	1(4.1)	3(9.4)	1(3.4)	6(30)	0.216
4	1-5 yr, no(%)	42(40)	11(45.8)	11(34.4)	13(44.8)	7(35)	1.0
5	5-12yr,no(%)	52(49.5)	13(54.1)	17(53.1)	15(51.7)	7(35)	0.43
6	Mean duration of fever, days(S.D)	5.09(2.3)	4.95(2.1)	5.25(2.5)	5.24(1.8)	4.8(2.7)	0.34

Most common manifestations were fever(100%), vomiting(81.9%), bleeding manifestations(77.14%), rashes(64.7%) and myalgia(62.8%).

Fever was continuous, biphasic, and intermittent in 70.4, 20.9 and 8 percentages respectively.

Myalgia was less commonly noted in DSS. But it was statistically not significant (P=0.47).

TABLE 2

CLINICAL FEATURES

No	**Feature**	**Total**	**DF**	**DFB**	**DHF**	**DSS**	**P value**
1	Fever,no(%)	105(100)	24(100)	32(100)	29(100)	20(100)	_
2	Myalgia,no(%)	66(62.8)	16(66.6)	23(71.8)	21(72.4)	6(30)	0.47
3	Headache,no(%)	22(20.9)	4(16.6)	5(15.6)	9(31)	4(20)	0.53
4	Abd.pain,no(%)	39(37.1)	5(20.8)	9(28.1)	19(65.5)	6(30)	0.41
5	Vomiting,no(%)	86(81.9)	16(66.6)	25(78.1)	25(86.2)	20(100)	0.0049
6	Altered sensorium,no(%)	68(64.7)	7(29.1)	17(53.1)	24(82.7)	20(100)	0.023

Vomiting was present in all DSS children (100%). When compared to DF group (66.6%) it is statistically significant (P=0.0049). All DSS had altered sensorium (100%). When compared to DF group (29.1%), it is statistically significant (P=0.023).

TABLE- 3

BLEEDING PROFILE

No	Feature	Total	DF	DFB	DHF	DSS	P value
1	Epistaxis, no(%)	2(1.9)	0(0)	1(3.1)	1(3.4)	0(0)	0.82
2	Malena, no(%)	12(11.4)	0(0)	6(18.75)	4(13.8)	2(10)	0.65
3	Hematemesis, no(%)	12(11.4)	0(0)	4(12.5)	4(13.8)	4(20)	0.73
4	IV bleed, no(%)	0(0)	0(0)	0(0)	0(0)	0(0)	_
5	Petechiae, no(%)	18(17.1)	0(0)	13(40.6)	5(17.2)	0(0)	0.61
6	Purpura, no(%)	1(0.95)	0(0)	1(3.1)	0(0)	0(0)	_
7	Ecchymosis,no(%)	0(0)	0(0)	0(0)	0(0)	0(0)	_
8	>1 site,no(%) (hematemesis+ petechiae)	36(34.3)	0(0)	7(21.9)	15(51.7)	14(70)	0.001
9	None	24	0	0	0	0	_

Out of 105 children ,81 had one or more form of bleeding manifestations. Bleeding from more than one site was the most common manifestation (P=0.001). Petechiae(17.1%),tourniquet +ve test(26.7%), hematemesis(11.4%), malena(11.4%), epistaxis(1.9%),purpura(0.95%) were other manifestations.

Hepatomegaly was present in 90% in DSS and 86.2% in DHF. It was statistically significant when compared with DF and DFB (P=0.0219).

TABLE 4 CLINICAL FEATURES

No	Feature	Total	DF	DFB	DHF	DSS	P value
1	Hepatomegaly, no(%)	53(50.5)	3(12.5)	7(21.9)	25(86.2)	18(90)	0.0219
2	Tourniquet +, no(%)	28(26.7)	0(0)	9(28.1)	12(41.4)	7(35)	0.35
3	Shock, no(%)	21(20)	1(4.1)	0(0)	0(0)	20(100)	0.001
4	3rd spacing, no(%)	49(46.6)	0(0)	0(0)	29(100)	20(100)	_

One DF child presented with shock. But there were no signs suggestive of plasma leakage. That child had improved with two boluses 0f normal saline.

Third spacing was seen in 49 children (46.6%).In DHF, 6 had only pleural effusion, 23 had both pleural effusion and ascites.

In DSS 2 had only pleural effusion, 18 had both pleural effusion and ascites. Pleural effusion was bilateral in 2 children.**TABLE: 5**

CLINICAL FEATURES

No	Feature	Total	DF	DFB	DHF	DSS	P value
1	Rash, no(%)	68(64.7)	15(62.5)	21(65.6)	18(62)	14(70)	0.57
2	Seizures,no(%)	10(9.5)	3(12.5)	1(3)	2(6.8)	4(20)	0.47
3	Loose stools, no(%)	9(8.5)	5(21)	1(3)	1(3)	2(10)	0.89
4	Bradycardia, no(%)	9(8.5)	4(16.6)	3(9.3)	2(6.8)	0(0)	0.78
5	Lymphadenopathy, no(%)	16(15.2)	12(50)	1(3.1)	2(6.8)	1(5)	0.46

Seizures (9.5%), loose stools (8.5%), lymphadenopathy (15.2%), relative bradycardia (8.5%) were less common manifestations. Rashes were seen in 64.7% of children.

Many children in this study were mildly anemic. Mean hemoglobin was slightly higher in DHF and DSS.

Mean Hb in DSS was 11.28g%. It was 10.02, 10.1, and 10.45 in DF, DFB, DHF respectively. But it was statistically not significant (P=0.27).

TABLE - 6

Hb & PCV

No	Feature	Total	DF	DFB	DHF	DSS	P value
1	Hb mean(S.D)	10.4(1)	10.02(1.05)	10.1(0.95)	10.45(0.9)	11.28(0.59)	0.27
2	Hematocrit mean(S.D)	34.06 (5.5)	30.8(2.6)	30.65(2.8)	37.27(6.9)	38.75(1.11)	0.0141

As many children were mildly anemic, the mean hematocrit value also relatively low. In DHF and DSS mean hematocrit was significantly higher than classical DF and DFB (P=0.0141). In DFB, DHF ,DSS low platelet counts correlate with bleeding manifestations(P=0.025).

SGOT and SGPT levels were elevated in all groups. Elevation of SGOT and SGPT were significantly higher in DHF and DSS when compared with classical dengue and DFB (P=0.001).

TABLE - 7

PLATELET COUNT (per cu.mm)

No	Feature	Total	DF	DFB	DHF	DSS	P value
1	>1 lakh,no(%)	3(2.8)	3(12.5)	0(0)	0(0)	0(0)	0.9
2	40000-1 lakh,no(%)	33(31.4)	17(70.8)	14(43.8)	2(6.9)	0(0)	0.37
3	20000-39999,no(%)	53(50.5)	4(16.6)	18(56.2)	19(65.5)	12(60)	0.025
4	<20000,no(%)	16(15.2)	0(0)	0(0)	8(27.6)	8(40)	0.013

TABLE - 8

SGOT & SGPT

No	Feature	Total	DF	DFB	DHF	DSS	P value
1	SGOT & SGOT,no(%) (>50IU/L)	75(71.4)	12(50)	17(53.1)	26(89.6)	20(100)	0.001

TABLE - 9

ULTRASOUND ABDOMEN

No	Feature	Total	DF	DFB	DHF	DSS	P value
1	Hepatomegaly,no(%)	56(53.3)	2(8.3)	6(18.75)	28(96.5)	20(100)	0.0017
2	Polyserositis,no(%)	16(15.2)	0(0)	1(3.1)	10(34.4)	5(25)	0.0032
3	Gall bladder wall thickening,no(%)	26(24.7)	0(0)	0(0)	13(44.8)	13(65)	0.001
4	Ascites,no(%)	41(39.04)	0(0)	0(0)	23(79.3)	18(90)	0.001
5	Normal study,no(%)	49(46.6)	22(91.6)	26(81.25)	1(3.4)	0(0)	0.001

In ultrasound abdomen, DHF (96.5%) and DSS (100%) had hepatomegaly. It is statistically significant when compared with DF and DFB (P=0.0017). Polyserositis also significantly more in DHF and DSS group(P=0.0032).

Gall bladder wall thickening was noted in 44.8% in DHF and 65% in DSS. No children in DF or DFB had gall bladder wall thickening. It is statistically significant (P=0.001). 49 children had no abnormalities in ultrasound abdomen. Children in DF and DFB had more reports of normal ultrasound abdomen (P=0.001).No children in DSS group had normal study.

TABLE-10

OUTCOME

No	Feature	Total	DF	DFB	DHF	DSS	P value
1	Recovery,no(%)	103(98.1)	24(100)	32(100)	29(100)	18(90)	0.0348
2	Death,no(%)	2(1.9)	0(0)	0(0)	0(0)	2(10)	0.0348

Out of 105 children, 103 were recovered from the illness. Two children from DSS group died. Both were brought to the hospital very late. Duration of hospital stay was less than 24 hours in both the children. Overall recovery rate was 98.1%. IN DF, DFB, DHF all children were recovered. Recovery rate in non-DSS group was significantly higher than DSS (P=0.0348). Mortality due to DSS was 10%. This is significantly higher than non-DSS group (P=0.0348). Overall mortality was 1.9%.

DISCUSSION

The relationship of dengue with India has been long and intense. The first recorded epidemic of clinically dengue like illness occurred at Madras (Chennai) in 1780 and the dengue virus was isolated for the first time almost simultaneously in Japan and Calcutta 1n 1943-44. Then it spread to all over the country. The first full blown epidemic of severe form of dengue occurred in North India in 1996. Every year the epidemiology and clinical manifestations are changing. Here I compare the clinical profile and outcome of dengue with other Indian and foreign studies.

Total of 105 cases of seropositive dengue children presented at Institute of Social Pediatrics were analyzed. According to WHO classification, Dengue fever(including DFB)(53.2%), Dengue hemorrhagic fever(27.6%), Dengue shock syndrome(19.04%) was seen.

Kabilan et al (Chennai 2001) reported DF(65.5%),DHF(11.2%), DSS(23.8%). Ratageri et al (Hubli 2003) reported DF(18%),DHF(60%),DSS(22%). Narayanan et al (Chennai 2001) reported DF(72.78%), DHF(18.6%),DSS(8.4%). Kalyanarooj et al(Indonesia) reported DF (including DFB) (53%), DHF(including DSS)(47%). In present study, DHF(including DSS) is 46.64%.Present study is comparable with other studies.

Incidence of DHF and DSS was increased when comparing the study by Narayanan (2001). It may be due to increasing endemicity, environmental factors and changing virulence of the viruses.

AGE

In present study, infants (10.4%), 1-5 years (40%), 6-12 years(49.5%) was observed. Kabilan et al reported 20%, 28.7% for infants and 1-5 years group. He reported that 6-15 years formed 51%. In present study, <5years were 50.4%. More than 5 years were 49.5%.Aggarwal et al reported 45% & 55% for the same groups. Infants are lesser in present study when comparing with Kabilan et al.

SEX

No	Study	Male(%)	Female(%)
1	Narayanan et al	52.4	47.6
2	Gomber et al	56	44
3	Aggarwal et al	60	40
4	Present study	53	47

It is comparable with other studies.

FEVER

Continuous (74%), Biphasic (22%), Intermittent (9%) was seen in the present study. Mean duration of fever was 5.09 days. Narayanan reported 4.9 days. It was lesser in DSS (4.8 days) and statistically not significant (P=0.34).

VOMITING

No	Study	Percentage
1	Kalyanarooj(Indonesia)	66
2	Ratageri(Hubli)	82
3	Narayanan(Chennai)	83
4	Present study	81.9

It is comparable to other studies. It was significantly more common in DSS group($P<0.05$).

HEMATEMESIS

No	Study	Percentage
1	Aggarwal et al	29
2	Narayanan et al	61
3	Ratageri et al	22
4	Present study	45.75

Bleeding from more than one site(hematemesis+ petechiae) was the most common in present study. Hematemesis was most common in other studies. Its percentage is variable in different studies.

HEADACHE

It was 28.8%(Narayanan), 77%(Kalyanarooj), 22%(Ratageri).

It is 20.9% in the present study. Younger kids may not complain this symptom. High percentage in Kalyanarooj's study may be due to different age composition.

ALTERED SENSORIUM

It was 65% by Ratageri and 23.7% by Narayanan. It is 64.7% in present study. Low percentage in Narayanan may be due to lesser DHF and DSS.

ABDOMINAL PAIN

It is 37.1% in present study and 34.5% in Kalyanarooj. Aggarwal reported 49%. He studied only DHF and DSS and may be the reason for high percentage.

HEPATOMEGALY

It was (72%) in Aggarwal, (52.5%) in Narayanan and (50.5%) in present study. Hepatomegaly was significantly more common in DHF and DSS in all studies.

TOURNIQUET TEST

It was 26.7% in Aggarwal, 25% in Gomber, 23.7% in Narayanan and 52% in Kalyanarooj(Indonesia). It is 26.7% in present study. High percentage in Indonesia may be due to difference in skin complexion and capillary fragility.

SHOCK

No	Study	Percentage
1	Aggarwal et al	33
2	Gomber et al	20
3	Narayanan et al	8.4
4	Kabilan et al	23.8
5	Ratageri et al	22
6	Present study	19.04

DSS was low in Narayanan et al. Due to increasing endemicity and changing epidemiology, DSS is in increasing trend.

THIRD SPACING

It is 100% in DHF and DSS in present study. Kalyanarooj reported 84% in DHF. Narayanan et al reported low percentage as there was low DHF and DSS.

LYMPHADENOPATHY

It is 15.2% in present study and 10.2% in Narayanan et al.

MEAN HEMOGLOBIN

It is 10.4g% in present study. Narayanan et al reported 10.8g%.

No	Classification	Present study	Narayanan et al
1	DF	10.02	10.8
2	DFB	10.1	11.1
3	DHF	10.45	10.3
4	DSS	11.28	11.4

MEAN HEMATOCRIT

Present study: 34.06%. Narayanan et al: 33.2%. Gomber et al reported 38.34%. In my study there is wide prevalence of mild anemia and low hematocrit. Mean hematocrit value was significantly higher in DHF and DSS group.

Hematocrit(mean)

No	Classification	Present study	Narayanan et al
1	DF	30.8	32.2
2	DFB	30.65	32.1
3	DHF	37.27	35.2
4	DSS	38.75	37.6

PLATELET COUNT

In present study, >1 lakh= 2.85%,

40000-1 lakh=31.4%,

20000-39999= 50.5%,

<20000= 15.2%.

Aggarwal et al reported,

>50000= 31%,

25000-50000=47%,

<25000= 22%.

Present study is comparable with Aggarwal et al.

SGOT & SGPT

They are elevated in 71.4%. Elevation in DHF and DSS was statistically more common than in DF and DFB. It was also seen in Aggarwal et al and Kalyanarooj et al.

ULTRASOUND ABDOMEN

No	Study	Ascites	GBWT	Hepatomegaly
1	Setiwan(Indonesia) Mild dengue	34%	32%	49%
2	Setiwan(Indonesia) Severe dengue	95%	95%	95%
3	Srikiatkhachom(Indonesia)	52%	43%	57%
4	Venkata sai (Chennai)	53%	100%	21%
5	Present study(DHF&DSS)	84.65%	54.9%	98.25%

GBWT= Gall bladder wall thickening.

In severe dengue(DHF & DSS), ascites, gall bladder wall thickening and hepatomegaly were significantly more common in present study($P<0.05$). The above studies also reveal the same. GBWT more than 5 mm in clinically suspected dengue cases signifies 91.7% specificity towards DHF and DSS.

MORTALITY

According to Halstead et al, mortality due to dengue in Asian countries is 0.5%-3.5% (if early recognition and appropriate treatment was instituted).

Mortality in my study is 1.9%.

No	Study	Mortality(%)
1	Kabra et al(1992)	12-13%
2	Srivastava et al (1990)	12-13%
3	Aggarwal et al (1996)	6%
4	Gomber et al (2001)	4.8%
5	Narayanan et al(2001)	3.3%
6	Kabilan et al(2001)	No mortality
7	Ratageri et al (2003)	No mortality
8	Present study	1.9%

Mortality rate is drastically reduced by early recognition, precise assessment and appropriate fluid management as per WHO protocol.

LIMITATIONS OF THE STUDY

1. Confirmation of dengue viral infection was not done. So, all the cases in the study are PROBABLE DENGUE according to WHO case definition.

2. Viral antibody titers were not done to diagnose primary and secondary dengue precisely.

3. Serotypes were not done. So the predominant serotype was not identified.

4. Treatment modalities like type of fluid used, need for inotrope support, ventilator support, need for blood products were not studied.

CONCLUSIONS

1 . Dengue fever is becoming more prevalent in India. Incidence of Dengue shock syndrome is increasing.

2. Vomiting, hematemesis, skin bleeds, altered sensorium , hepatomegaly, elevated SGOT, SGPT, gall bladder wall thickening, ascites, pleural effusion following the period of fever defervescence strongly indicate Dengue hemorrhagic fever and dengue shock syndrome.

3. The bleeding in dengue is not purely due to thrombocytopenia. It is due to multiple etiologies including vascular changes.

4. No role for prophylactic platelet transfusion.

5. Early recognition, precise assessment and appropriate treatment have reduced the mortality.

6. Parental health education about the fever defervescence and early referral may prevent deaths due to dengue.

ANNEXURES

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ABBREVIATIONS

DF	:	Dengue fever
DFB	:	Dengue fever with unusual bleeds
DHF	:	Dengue hemorrhagic fever
DSS	:	Dengue shock syndrome
WHO	:	World health organization
ELISA	:	Enzyme linked immunosorbent assay
Hb	:	Hemoglbin
PCV	:	Packed cell volume
SGOT	:	Serum Glutamate Oxalo-acetate Transaminase
SGPT	:	Serum Glutamate Pyruvate Transaminase
NS proteins	:	Non-structural proteins
FFP	:	Fresh Frozen Plasma
GBWT	:	Gall bladder wall thickening.

PROFORMA

Name

Age

Sex

IP No

Address

Date of admission

Date of discharge

Fever type

Myalgia

Head ache

Abdominal pain

Vomiting

Epistaxis

Malena

Haemetemesis

Venepuncture bleed

Rash

Tourniquet test

Altered sensorium

Seizures

Loose stools

Relative bradycardia

Hepatomegaly

Shock

Third spacing

Lymphadenopathy

Hb

PCV

TC

Platelet count

IgM

IgG

SGOT

SGPT

CXR

USG Abdomen

WHO Classification

Outcome.

KEY TO MASTER CHART

Age(in years) :

Sex : M/F

Fever type : 1.continuous 2.biphasic 3.intermittent

Myalgia : 1.yes 2.no 3.not applicable

Headache : 1.yes 2.no 3.not applicable

Abdominal pain: 1. yes 2. no 3. not applicable

Vomiting : 1.yes 2.no

Bleeding manifestations : 1.epistaxis 2.malena 3.haematemesis 4.venepuncture bleed 5.petechiae 6.purpura 7.ecchymosis 8.bleeding from more than one site(hematemesis+petechiae).

Rash : 1.yes 2.no

Tourniquet test : 1.positive 2.negative

Sensorium : 1.lethargy 2.drowsy 3.obtundation 4.stupor 5.coma

Seizures : 1.generalised 2.focal 3.none

Loose stools : 1.yes 2.no

Relative bradycardia : 1. Yes 2. no

Hepatomegaly : 1.yes 2.no

Shock : 1. yes 2.no

Third spacing : 1.ascites 2.pleural effusion 3.both 4.none

Lymphadenopathy : 1.yes 2.no

Hemoglobin :

Hematocrit :

Total count :

Platelet count : 1.<20000/cu.mm 2.20000 to 40000/cu.mm 3.>40000 to < 1 lakh/cu.mm 4. > 1 lakh/cu.mm

Ig M :1. positive 2. negative

Ig G : 1.positive 2.negative

SGOT >50 IU/L : 1.yes 2. no

SGPT >50 IU/L : 1.yes 2.no

Alkaline phosphatase > 200 IU/L : 1.yes 2.no

Pleural effusion in CXR : 1.yes 2.no

USG Abdomen : 1.hepatomegaly 2.hepatomegaly+polyserositis 3.hepatomegaly+polyserositis+gall bladder wall edema

4. hepatomegaly+ gall bladder wall edema

WHO classification : 1.Dengue fever

2.Dengue fever with unusual bleed

3.Dengue hemorrhagic fever

4.Dengue shock syndrome.

Outcome : 1.recovered 2.died.

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