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OVERVIEW ON DENGUE HEAMORRAGIC FEVER

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Abstract - *The flaviviridae family, which is an arthopoda, is mostly responsible for flaccid fever. The word denga, which signifies fever and haemorrhages, is borrowed from Africa. The virus is typically transmitted through mosquito bites, specifically those from the Aedes Aegypti species. The rainy season is when this disease is most prevalent. DHF causes cutaneous and intestinal haemorrhages as a result of thrombocytopenia, hemoconcentration, hypovolumic changes, and neurologic abnormalities. DHF causes focal haemorrhages, congestion that increases vascular permeability, oedema in a specific organ, coagulopathy with thrombocytopenia, and hemoconcentration in the organs that are affected by the virus. Serologic testing is used to detect it. Symptoms of DHF include severe malaise, high fever, and nausea, vomiting, athralgia, flushing, and severe abdominal pain. DHF NASAIDS PCM (antipyretic) and non-pharmacological treatment are also incorporated in the management of DHF.*

***Key Words*: NSAIDS, Thromobocytopenia, Haemorrhages, and Dengue fever.**

1. INTRODUCTION

The most prevalent arthropod infection, dengue fever, is brought on by the flaviviridae family. Fever is the result[1]. The word "Denga" is an African word that signifies fever with haemorrhages and means fever. The virus that causes it is most frequently spread via the bite of the Aedes aegypti mosquito. This virus spreads most quickly during the rainy season, when mosquito populations are at their highest[2]. It is correlated with climatic and environmental factors and exhibits both geographical and temporal patterns[3]. Major routes run through the tropical and subtropical regions[4].

1.1 Epidemiology:

Dengue illness has afflicted 50 million people worldwide, with 20,000 deaths and 50,000 severe cases annually. For dengue fever, there is no vaccination available[5].

1.2 DHF

DHF is a severe kind of fever that is almost always deadly and is characterised by cutaneous and intestinal bleeding brought on by thrombocytopenia, hemoconcentration, hypovolemic shock, and neurological abnormalities. Children under the age of 15 are the most affected by it. Monocytes, lymphocytes, and endothelial cells in the blood are affected by dengue. It results in thrombocytopenia and complement activation, which together make up consumptive coagulopathy. This procedure moves forward considerably more quickly, taking only a few hours. Starting the appropriate treatment at this point will result in a rapid and significant recovery, but in untreated instances, dengue shock syndrome will develop, and death may result.

PATHOLOGICAL CHANGES

The DHF-affected organs exhibit specific changes in this type of fever, including focal haemorrhages, congestion that increases vascular permeability and results in oedema in particular organs, coagulopathy with thrombocytopenia, and hemoconcentration.

DIAGNOSIS

DHF is confirmed by immunofluorescence methods, monoclonal antibodies, rapid methods such reverse transcriptase-PCR and fluorogenic-ELISA, and serologic testing for the identification of antibodies[6].

1.3 DENGUE FEVER

Either a primary infection or a secondary infection results from dengue fever. Hyperpyrexia, severe headaches (especially in the retro-orbital area), athralgia, myalgia, anorexia, abdominal discomfort, and occasionally macular papular rashes are unanticipated symptoms. The fever can be biphasic[7,8] and it lasts for 2–7 days. Coryza is particularly common in children and may be the primary symptom[9]. Dengue fever recovery can be prolonged, especially in adults, although it can also be monotonous[10]. High temperature, severe headache (mostly in the retroorbital area), flushing, myalgia, athralgia, vomiting, anorexia, and abrupt stomach discomfort are all clinical signs of DHF[11,12]. Indicators of bleeding include nasal bleeding, gingivitis, bruises (ecchymosis), vomiting blood, dark blood in the stool, and spotting or menorrhagia in females. Indicators of plasma leakage include circulation abnormalities (low BP), quick heartbeat, and bruising, low pulse pressure, slow capillary refill time, pleural effusion, ascites, and occasionally pericarditis can lead to complications such as neurological diseases, brain disease (encephalopathy), brain inflammation, persistent liver failure, heart muscle inflammation, and consumptive coagulopathy.

Dengue Hemorrhagic Fever

Although it can affect adults, DHF is primarily a condition of children under the age of 15. A number of vague signs and symptoms, including a sudden onset of fever that typically lasts 2 to 7 days, describe it. It might be challenging to identify DHF from dengue fever and other tropical infections during the acute stage of the illness. Measles, rubella, influenza, typhoid, leptospirosis, malaria, and other viral hemorrhagic fevers should be included in the differential diagnosis during the acute phase of the illness, any other illness that can manifest during the acute stage as an undifferentiated viral condition. Upper respiratory symptoms in children are usually caused by concomitant infections with several viruses and bacteria. During the acute stage, there is no pathognomonic sign or symptom for DHF; however, when the fever subsides, distinctive signs of plasma leakage occur, often allowing for a precise clinical diagnosis.

Defervescence is when DHF enters its critical stage, however symptoms of circulatory failure or hemorrhagic manifestations might appear up to 24 hours before or after the temperature reaches normal or below. Indicators of a vascular leak in the patient's blood include thrombocytopenia (platelet count, 100,000/mm3) and hemoconcentration compared to baseline.

syndrome. Skin haemorrhages such petechiae, purpuric lesions, and ecchymoses are typical hemorrhagic symptoms. Less commonly, epistaxis, bleeding gums, GI haemorrhage, and hematuria happen. The tourniquet test, which shows that the patient's capillaries are more fragile, may aid the doctor in making a diagnosis. The most prevalent hemorrhagic symptom is scattered petechiae, which most frequently affects the limbs but can also affect the trunk, other body regions, and the face in those with severe dengue shock syndrome (DSS). Although purpuric lesions can develop everywhere in the body, they often occur where venipuncture is performed. Large ecchymotic lesions may form on the trunk and extremities in some individuals, whereas venipuncture sites in other patients may bleed actively, sometimes excessively. Patients who are more seriously unwell suffer GI bleeding. Although patients may experience extensive, open upper GI bleeding as well, frequently before to the start of shock, the classic hematemesis with coffee-ground vomitus and melena typically occurs after protracted shock. Without early detection and appropriate treatment, some patients experience shock from blood loss, which may be mild or severe. More commonly, shock is caused by plasma leakage; it may be mild and transient or progress to profound shock with undetectable pulse and blood pressure. Children with profound shock are often somnolent, exhibit petechiae on the face, and have perioral cyanosis.

Patients with severe DHF or DSS typically experience a fever and vague constitutional symptoms for a few days before their health abruptly deteriorates. The patient's skin may turn chilly, blotchy, and congested during, right before, or right after the temperature drop. Circumoral cyanosis is usually seen, and the pulse becomes weak and fast. Although some patients first seem sluggish, they quickly transition into a severe stage of shock after becoming restless. They typically feel severe stomach discomfort just before going into shock.

All indications and symptoms disappear in people with moderate DHF quickly after the temperature goes down. However, the onset of fever may be followed by excessive sweating, slight variations in blood pressure and pulse rate, coldness in the extremities, and skin congestion. These alterations represent brief, minor circulatory disruptions brought on by plasma leakage. Usually, patients get well on their own or after receiving fluid and electrolyte treatment. Without proper care, patients who are in shock risk dying. The patient may pass away within 8 to 24 hours of going into shock, however recovery from shock is typically swift after receiving antishock treatment. With or without shock, convalescence for individuals with DHF is often brief and uncomplicated. Once the first shock has passed, even those with undetectable pulse and blood pressure will usually recover within 2 to 3 days.

Leukopenia is typical, similar to dengue fever, and thrombocytopenia and hemoconcentration are ongoing observations in DHF and DSS. It is typical to find a platelet count of 100,000/mm3 between days 3 and 8 of sickness. In traditional DHF, hemoconcentration, a sign of plasma leakage, is usually always present, although it is more severe in shock patients. Hepatomegaly is a typical, though not always present, finding. Most individuals with proven DHF and DSS have enlarged livers in various nations. Hepatomegaly in other nations, however, fluctuates from one pandemic to another, suggesting that liver involvement might vary depending on the virus's strain and/or serotype. Elevated levels of liver enzymes are typical. An abrupt increase in vascular permeability that causes plasma to leak into the extravascular compartment, causing hemoconcentration and a drop in blood pressure, is the main pathophysiologic aberration found in DHF and DSS. Studies on plasma volume have revealed a drop of more than 20% in serious instances. Serous effusion discovered postmortem, pleural effusion shown on an X-ray, hemoconcentration, and hypoproteinemia are all supporting evidence of plasma leakage. Fatality rates can be reduced to 1% or less with early diagnosis, vigorous fluid replacement treatment, and competent nursing care. Individuals with moderate DHF and DSS can utilise normal saline or lactated Ringer's solution; however, patients with severe cases may require plasma or plasma expanders. Information on the efficient handling of DHF and DSS has previously been provided. Since there are no obvious destructive vascular lesions, it is likely that a short-acting mediator is to blame for the temporary functional vascular alterations. The extravasated fluid is

quickly reabsorbed when the patient is stabilised and starts to recover, which results in a decrease in the hematocrit.

Vascular abnormalities, thrombocytopenia, and coagulation issues all contribute to hemostatic alterations in DHF and DSS. The majority of DHF patients have abnormal coagulograms, increased vascular fragility, and thrombocytopenia, all of which suggest disseminated intravascular coagulation. Concomitant thrombocytopenia, a prolonged partial thromboplastin time, a decreased fibrinogen level, and increased levels of fibrinogen degradation products are additional signs of disseminated intravascular coagulation. The majority of patients who pass away had GI bleeding, according to autopsies.[21]

1.4 LABORATORY FINDING S IN DHF

Hematological analysis: Thrombocytopenia (100*109/L), abnormal lymphocytosis >15%, odd coagulation blood profile, drop in WBC quantity during early illness (extended activated partial thromboplastin time, prothrombin time, raised fibrinogen degradation products and lower serum complement range.

Investigating biologically: acidosis, elevated liner enzymes, and hypoalbunemia[13].

PATHOGENESIS OF DHF

Dengue can be caused by any of its viral serotypes, but when one is infected, it gives rise to future defence immunity against that serotype but not for others. Additionally, when a different serotype is infected for the second time, a more severe infection occurs. This is due to an occurrence known as antibody dependent enhancement, in which the antibody from one serotype infection amplifies infection with a different serotype[14]. While there is currently no proof that certain persons can cause symptoms of illness, active study has been done in this area. The dengue virus enters the human body by the bite of an infected person, where it replicates inside macrophages, monocytes, and B cells. Additionally, it is known that mast cells, dendritic cells, and endothelial cells can get infected[15,16,17]. The virus must mature for 7–10 days before it may start an infection. Patient exhibits signs of febrile illness during the viremia phase, which is followed by the leakage phase, which results in bleeding (DHF) for dengue shock syndrome. When viruses appear in plasma and reach maximal plasma level, the disease worsens[18].

Factors Responsible for the Increased Incidence

Unprecedented worldwide population expansion and the ensuing unplanned and unregulated urbanisation, particularly in tropical developing nations, have been two key contributing reasons. Unplanned urbanisation has resulted in subpar housing, overcrowding, and a decline in water, sewer, and waste management systems, which have created the perfect environment for increasing mosquito-borne disease transmission in tropical metropolitan areas.

The absence of efficient mosquito control in places where dengue is endemic has been a third significant contributing factor.[21]

2. MANAGEMENT OF DENGUE FEVER

Dengue fever and the febrile stage of DHF are closely associated in terms of control. PCM is the only antipyretic that is intended, unlike NSAIDS like aspirin and diclofenac sodium might cause GI bleeding or cause gastrointestinal discomfort. If the fever continues to be high after the administration of PCM, teped, sponging is indicated as the progression to hepatic damage associated with dengue virus infection may be worse. The dose of PCM (60 mg/kg/day) should not be increased. If a soft diet is refused, non-pharmacological therapy is indicated, such as switching oral rehydration solution.

Cimetidine is prescribed to patients who have stomach bleeding or a low platelet count. Domperidone, an antiemetic, is used to treat vomiting. Except for patients with severe vomiting or dehydration, IV fluid management is not advised for patients in the febrile phase. Platelet count and packed cell volume should be performed daily as soon as the fever starts on the third day in order to determine if the patient is entering the plasma leaking phase or not. Significant plasma loss is defined as platelet count 100*109/L and an increase in packed cell volume of >20%[19].

The following is the Halliday and Segar formula for the fluid demand in DHF[20]:

• Body weight under 10 kg: 100 mg/kg

• Body weight between 10 and 20 kg: 1000 ml plus 50 ml for each kg over 10 kg

• For body weights of 20 kg or more, add 20 ml to 1500 ml.

2.1 Vaccine Development

The first candidate dengue vaccines were developed shortly after the viruses were first isolated by Japanese and American scientists. Despite considerable work over the years, an effective safe vaccine was never developed. The World Health Organization designated the development of a tetravalent dengue vaccine a priority for the most cost-effective approach to dengue prevention. Effective vaccination to prevent DHF will most probably require a tetravalent vaccine, because epidemiologic studies have shown that preexisting heterotypic dengue antibody is a risk factor for DHF. In recent years, significant work has been made in creating a vaccine for dengue and DHF with the help of the World Health Organization. Phase I and II studies in Thailand have examined promising candidate attenuated

vaccine viruses in monovalent, bivalent, trivalent, and tetravalent formulations. The tetravalent vaccine formulation is presently conducting follow-up phase I trials in the United States, and a commercialization agreement has been struck. A current evaluation of the live attenuated dengue vaccine's development is available.[21]

CONCLUSION

Reviewing dengue hemorrhagic fever's impact on public health, which has made it one of the most prevalent illnesses, is the key goal. This review article is concerned with different clinical manifestations, diagnoses, and effective treatment strategies. The development of a vaccine and an antiviral medication regimen are the next directions in the fight against this terrible illness.

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