A Review on Epidemiology, Clinical Manifestation and Diagnostic Approach of Dengue in Bangladesh Perspective

SM NAZNIN[a], MM HOSSAIN[b], QS IFTEKHAR[c], T AHASAN[d]

Abstract:

Background: Dengue is an arboviral disease caused by dengue virus; single positive stranded RNA virus of the family Flaviviridae. Symptomatic dengue infection causes a wide range of clinical manifestations; from mild dengue fever (DF) to potentially fatal disease, such as dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS). Dengue is endemic in Bangladesh with recurrent outbreak and is one of the major public health concerns in current period. Therefore; we conducted a literature review to analyze demography, epidemiology, pathogenesis, clinical feature and diagnosis of dengue virus infection.

Methods: According to the PRISMA guidelines, the references were selected from PubMed, Web of Science and Google Scholar database using search strings containing a combination of terms that included"dengue", "Bangladesh", "epidemiology", "outbreak"," pathogenesis", "clinical manifestation", "demography "and "diagnosis". Quality of references was evaluated by independent contributors.

Results: About 167,700 confirmed dengue cases were reported at 16'september'2023 in Bangladesh. Although dengue is endemic in Bangladesh, the current dengue surge is unusual in terms of seasonality and the early sharp increase in comparison to previous years, where the surge started around –late June. Plasma leakages are the main pathophysiological hallmark that distinguishes DHF from DF. Severe plasma leakage can result in hypovolemic shock. Various factors are thought to impact disease presentation and severity. Virus segregation in cell cultures, nucleic acid demonstration by polymerase chain reaction (PCR), and serological detection of viral antigens (such as NS1) or particular antibodies are the preferred microbiological assays for dengue detection. Currently, no specific drugs and licensed vaccines are available to treat dengue disease in any of its clinical presentations for all age group.

Conclusion: Understanding the clinical manifestation of dengue infection, prompt diagnosis, appropriate treatment, active and continuous surveillance of cases and vectors are the essential determinants for dengue prevention, control and reducing fatality rate.

Key word: Dengue, Bangladesh, epidemiology, outbreak, pathogenesis, clinical manifestation, demography and diagnosis.

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Introduction:

Dengue is a febrile illness with clinical manifestations ranging from asymptomatic infection to severe infection with multi-organ dysfunction. [1,2]. it is one of the most important and fastest-growing mosquito-borne viral infections in the world today and a disease of major public health concern owing to potential lethal outcomes of severe infection. [3, 4] Dengue is hyperendemic in tropical and subtropical climates worldwide, mostly in urban and semi-urban areas. Global incidence of dengue has grown exponentially in recent years and nearly half of the world's population is now at risk. Many factors have influenced the global rise of dengue, including population growth, high population density, unplanned rapid urbanization and construction, climate change, absence of reliable piped water, and ineffective vector control strategies, enormous shift to urban living, increase in tourism, business related travel and global

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deployment of military and international non-governmental organizations.[4]

The World Health Organization (WHO) considers dengue as a major global public health challenge in the tropic and subtropic nations. Dengue has seen a 30-fold upsurge worldwide between 1960 and 2023, due to increased population growth rate, global warming, unplanned urbanization, inefficient mosquito control, frequent air travel, and lack of health care facilities. Two and a half billion people reside in dengue-endemic regions and roughly 400 million infections occurring per year, with a mortality rate surpassing 5–20% in some areas.[4]

The clinical manifestation and outcome of patients with dengue still varies widely from country to country. This is particularly true as dengue emerges in new areas of the world where the public health systems are not experienced in the prevention of the disease or the surge capacity in clinics and hospitals is not available to deal with the sudden increase in the number of patients and the clinical experience is limited. In these settings, mortality and morbidity are often higher than in other regions where dengue has been endemic for decades.[4]

Bangladesh has experienced sporadic dengue fever outbreaks since 1964 until the first large outbreak in 2000, with more than 5500 confirmed cases. Dengue outbreak usually coincides with the warmer months and monsoon season (May-September). At 16 September 2023 nearly 167700 confirmed dengue cases were reported ,exceeding by over 66300; the previous highest record of around 101300 for the entire 2019 according to the report of DGHS. The dengue virus has affected all 64 districts of Bangladesh with more prevalence in the districts of Dhaka, Chattogram, Barisal, Patuakhali, Lakshmipur, Pirojpur, Chandpur, Manikgang, Cumilla and Faridpur.[5] WHO highlights that the prevention of mosquito bite is the best way to avoid getting dengue.

Aim of the review:

Dengue infection becomes potentially lethal to affected individual according to severity. This infection have become changed its character with time. My aim of this review study is to highlight the current pictures of dengue infection in Bangladesh perspectives so that local government authority, national NGOs and international humanitarian organizations have taken correct initiatives to raise awareness regarding dengue preventive measures among the public of Bangladesh and reduce the morbidity and mortality rate of people.

Methods:

Search strategy

A narrative literature review was conducted on the current status of demography, epidemiology, clinical spectrum and diagnostic approach of dengue in Bangladesh perspective. However, we did not register any protocol for this review. Selected references were from PubMed, Web of Science and Google Scholar database using search strings containing a combination of terms that included dengue fever, pathogenesis, clinical aspect and diagnosis. For this purpose, Scopus and PubMed were searched using the keyword "Dengue AND Bangladesh". Bangladeshi articles were searched in the BanglaJol database (an exclusive database of Bangladeshi Journal) with a combination of "Dengue", "Bangladesh", "epidemiology", "outbreak"," pathogenesis", "clinical manifestation", "demography "and "diagnosis .

Eligibility criteria

In this study, specific criteria were used to select relevant articles for analysis. The inclusion criteria were: (i) articles describing the epidemiology, clinical manifestations, serotype/genotype, risk factors, clinical features, diagnostic approach and knowledge and awareness regarding dengue in Bangladesh and (ii) articles published in English. The exclusion criteria were: (i) non-peer-reviewed articles (such as editorials and comments) and (ii) articles published in other languages.

Selection of studies and data extraction

Two independent authors evaluated the level of data quality from the selected literatures. Disagreements were resolved by joint discussion and consensus initially, 183 articles were identified via initial searching after removing duplicates and 125 were selected after screening title and abstract. We excluded 83 articles after reading the full-text according to the exclusion criteria and finally, 42 articles were included and discussed in this review. Ethics approval and informed consent were not required for this study. The systemic search covered the publications dates from January '1992 to 15 October' 2023.

The final search results were inserted into Excel and duplicates were removed. Two reviewers (MMH and

QSI) screened the title and abstract. Full texts of the primarily selected articles were also screened thoroughly. Any discrepancies found during the selection of studies were resolved through discussion and consensus of the two authors which were then evaluated by a third author (TA).

Result:

Demography:

Gender distribution showed a clear male predominance in all the dengue outbreaks reported in Bangladesh. The proportion of male cases was almost double compared to females in all studies Male-to-female ratio was as high as 2.7[6]. In adolescents and adults, significant male excess was also noted in six other culturally and economically diverse Asian countries. However, the difference was not significant in pediatric groups[7]. A study among children in Bangladesh also reported a similar result[9]. While male predominance was also reported in most studies from India, few studies showed variable distribution[9]. This is in contrast to findings in South America, where female cases were equal to or greater than males[10]. The clinical significance of such gender differences is not clear. Therefore, this difference could reflect case selection bias as most studies were hospital-based, with male patients prevalent in developing countries, such as Bangladesh. Another possibility could be the cultural aspect (dress code), where females are generally covered in South Asia.

Adult population is commonly affected by dengue in Bangladesh. During the first epidemic in 2000, more than 80% of cases were adults (>18 years of age); the peak number of cases occurred between 18 and 33 years of age [11]. Likewise, the majority (62%) of the confirmed case belonged to the 16–30 age group, with a mean age of 29 years in the 2002 outbreak[6]. Older adolescents and young adults also comprised the majority of the cases in 2016 (21–40; 55%), 2018 (15–29; 65%), and 2019 (21–40; 50%) outbreaks[12-14]. A similar result was reported in Sri Lanka in 2018 [15] and Ethiopia in 2017 [16]. While studies conducted in different parts of India also noted a predominance of young adults [9], the first major dengue outbreak in Delhi in 1996 mainly affected the 5–12-year-old age group[17]. Similarly, surveillance data in Puerto Rico reported the highest incidence between 10 and 19 years during the 1994 and 1995 outbreaks[18]. This suggests that dengue is experiencing a demographic shift to older ages over the last decade.

Among pediatric cases below 15 years, dengue affected mostly older children in Bangladesh. A hospital-based study conducted during the 2019 outbreak found that the majority (46.1%) of the children belonged to the 10–14 age group with a mean age of 8.8 years [8]. A similar observation was also noted in other Asian countries [19]. The disproportionately high exposure to infected mosquitoes among children >6 years could explain this as children begin attending elementary school and spend more time in crowded places at that age[20].

Epidemiology:

Dengue is one of the most common tropical diseases affecting humans. Dengue has become a major international problem in public health in recent decades. The World Health Organization (WHO) estimates that around 2.5–3 billion people are presently living in dengue transmitted zones[5]. Many factors have influenced the global rise of dengue, including population growth, high population density, unplanned rapid urbanization and construction, climate change, absence of reliable piped water, and ineffective vector control strategies[5]. The rapid global spread of dengue is also associated with increased human mobility through air travel; 75% of the global dengue burden lies in Southeast Asia and the Western Pacific region[8]. The incidence of overall global dengue virus (DENV) infection has also increased rapidly in the last two decades; 505,430 cases were reported in 2000, while over 2,400,138 and 3,312,040 cases have been reported in 2010 and 2015, respectively. The number of deaths has also increased from 960 to more than 4032 between 2000 and 2015 [21]. Each year, an estimated 100–400 million infections occur, and over 80% of these infections are generally mild and asymptomatic[21]. In line with global trends, the incidence of dengue has also dramatically increased in Bangladesh. A recent study estimated that in Bangladesh, 40 million [range: 34.3–47.2] people are infected nationally, with 2.4 million [range: 1.3–4.5] annual infections[29]. The first dengue outbreak in Bangladesh was reported in 1964 in the East Pakistan, and the term Dacca fever was coined[30, 31]. The first official dengue outbreak in Bangladesh was reported in 2000, with 5551 cases and 93 deaths reported[32]. Since then, dengue has become endemic in Bangladesh. In

2018, more than 10,000 cases of dengue were reported for the first time. Notably, in 2019, Bangladesh witnessed one of the largest dengue epidemics in its history with 101,354 dengue cases and 164 dengue-related deaths being reported[33]. In 2020, Bangladesh reported 1405 dengue cases and only three confirmed dengue-related deaths[34]. In 2021, 28,429 dengue cases and 105 dengue-related deaths were reported .In the year 2022, an increasing trend of dengue outbreaks was observed in many countries, including Bangladesh. As of 23 November 2022, a total of 3,643,763 dengue cases and 3380 dengue-related deaths were reported globally[35]. As of 10 December 2022, a total of 60,078 dengue cases and 266 dengue-related deaths were reported in Bangladesh, and the 2022 outbreak is the second-largest outbreak since 2000[36].

Importantly, regional variation in dengue occurrence was observed both in 2019 and 2022. In particular, the Directorate General of Health Services (DGHS), Bangladesh reports data on dengue cases and deaths separately for Dhaka City and the Dhaka Division excluding Dhaka City; however, to show division-wise dengue cases and death occurrence, we used Dhaka Division data that also included data for Dhaka City In 2019, the highest occurrence of dengue cases was observed in Dhaka Division, followed by the Khulna, Chattogram, Barishal, Rajshahi, Mymensingh, Rangpur, and Sylhet divisions . In 2022, the highest occurrence of dengue cases was again observed in the Dhaka Division, followed by Chattogram, Khulna, Barishal, Rajshahi, Mymensingh, Rangpur, and Sylhet, suggesting that Dhaka Division—in particular, Dhaka City—was the center point for dengue outbreak. The number of dengue-related deaths increased in 2022 compared to those in 2022. However, it is likely that the coronavirus disease 2019 (COVID-19) pandemic may have hampered dengue case reporting, since the first reported COVID-19 case in Bangladesh was on 8 March 2020 [17]. Notably, compared to the previous four years (2018–2021), as on 24 July 2022, there was an acute surge in dengue, resulting in 7687 confirmed dengue cases and six dengue-related deaths (case fatality rate, 0.08%) in the Rohingya refugee/Forcibly Displaced Myanmar Nationals camps in Cox's Bazar district, Bangladesh .

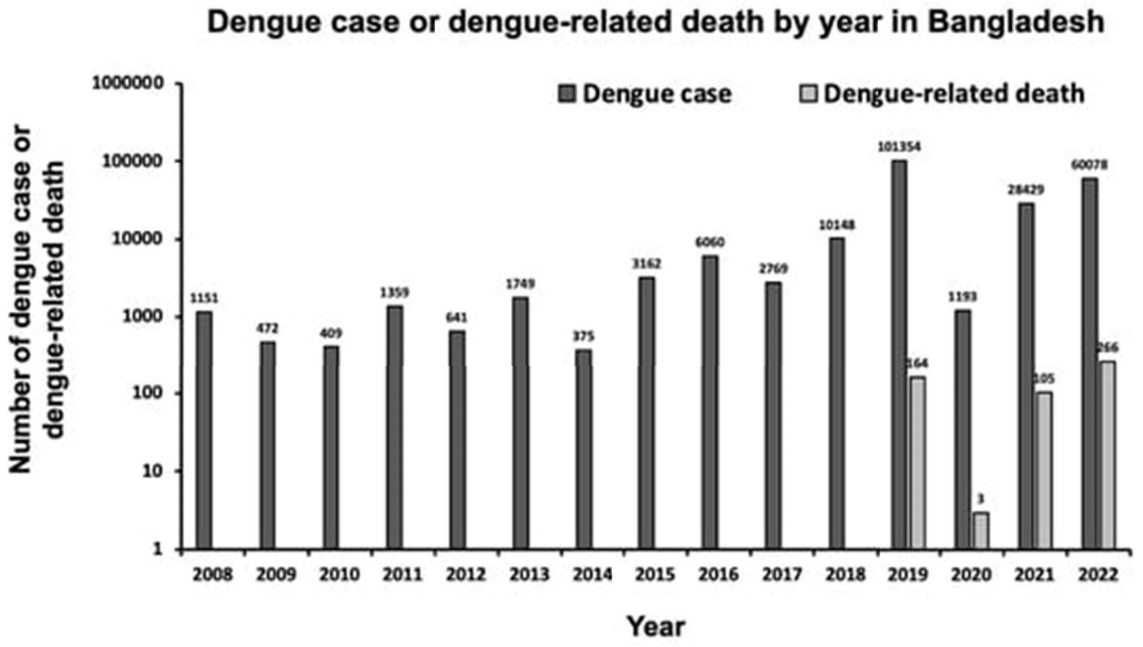

Fig.-1: *Number of reported dengue case and dengue-related death per year in Bangladesh between 2008 and 10 December 2022 (Courtesy: Journal of Tropical Medicine and Infectious Disease)*

Dengue Virus (DENV):

Dengue is an acute febrile disease triggered by an infection with dengue virus (DENV). Dengue virus (DENV) is a small, spherical, single-stranded RNA virus with 10,700 bases.The dengue virus, a member of the genus *Flavivirus* of the family Flaviviridae; it is a single positive-stranded RNA *flaviviruses* ; an arthropode-borne virus that includes four different serotypes (DEN-1, DEN-2, DEN-3, and DEN-4) depending on differences in the viral structural and non-structural proteins. Human become infected with dengue through the bite of DENV-carrying female *Aedes* mosquitoes, including *Aedes albopictus* and *Aedes aegypti.* Subsequent infection with distinctive serotype of DENVs has been associated with increase the risk of severe complications[1].

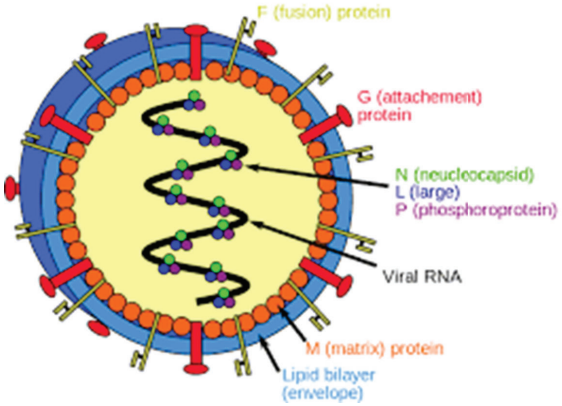

Fig.-2: *Virological structure of dengue virus*

Due to mutations of the virus, the severity of the infection varies from time to time where genotypes have been described, eg A and B in DEN3. Infection with each serotype confers lifelong immunity for the causative serotype, but not for the other serotypes. On the contrary, reinfection with a different serotype causes severe disease. In a given region, periodic outbreaks occur due to different serotypes over decades, thus development of complete herd immunity for all four serotypes in the community is not achievable and the disease may remain without natural elimination.[3]

Etiopathogenesis:

DF is a severe flu-like infection that involves individuals of all age groups (infants, children, adolescents, and adults) [37] Transmission among human beings occurs by the mosquito *Aedes aegypti* and chiefly occurs during the rainy season.[38] The proposed etiologies for dengue virus infection are viral replication, primarily in macrophages[39] followed by direct skin infection by the virus[40] which leads to immunological and chemical-mediated mechanism induced by host–viral interaction.[40]

Dengue virus gains entry into the host organism through the skin following an infected mosquito bite. Humoral, cellular, and innate host immune responses are implicated in the progression of the illness and the more severe clinical signs occur following the rapid clearance of the virus from the host organism. Hence, the most severe clinical presentation during the infection course does not correlate with increasing viral load.[41] Iterations in endothelial micro vascular permeability and thromboregulatory mechanisms lead to an increased loss of protein and plasma. Proposed theories suggest that endothelial cell activation caused by monocytes, T-cells, the complement system, and various inflammatory molecules mediate plasma leakage. Thrombocytopenia may be related to alterations in megakaryocytopoiesis, manifested by infection of human hematopoietic cells and compromised progenitor cell growth. This may cause platelet dysfunction, damage, or depletion, leading to significant hemorrhages. [42]

Vector Characteristic and immune pathogenesis:

Dengue is transmitted from person to person via the bite of an infected mosquito. Of these, the primary vector is *Aedes aegypti*, which is a highly domestic mosquito, a day biter, breeding in water containers in peri-domestic areas. Its eggs could survive without desiccation in dried condition for months and with the first opportunity of contact with water, the life cycle begins. *Aedes albopictus* is a secondary dengue vector confined to a few regions in the world and is called 'tiger mosquito' due to its characteristic morphology. The following pictures show these two main *Aedes* mosquitoes and their unique body features.[3]

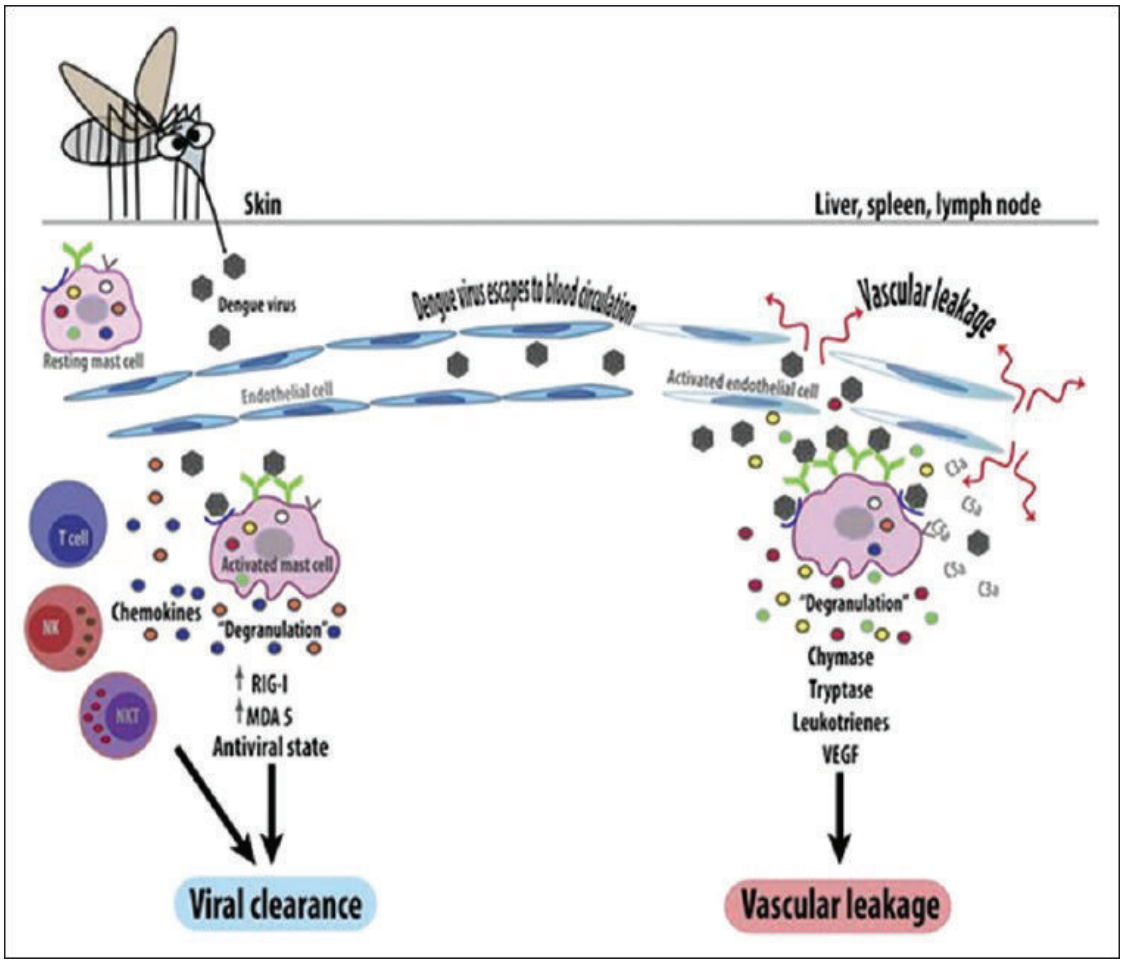

Fig.-3: *Diagrammatic representation of the pathogenesis of dengue.*

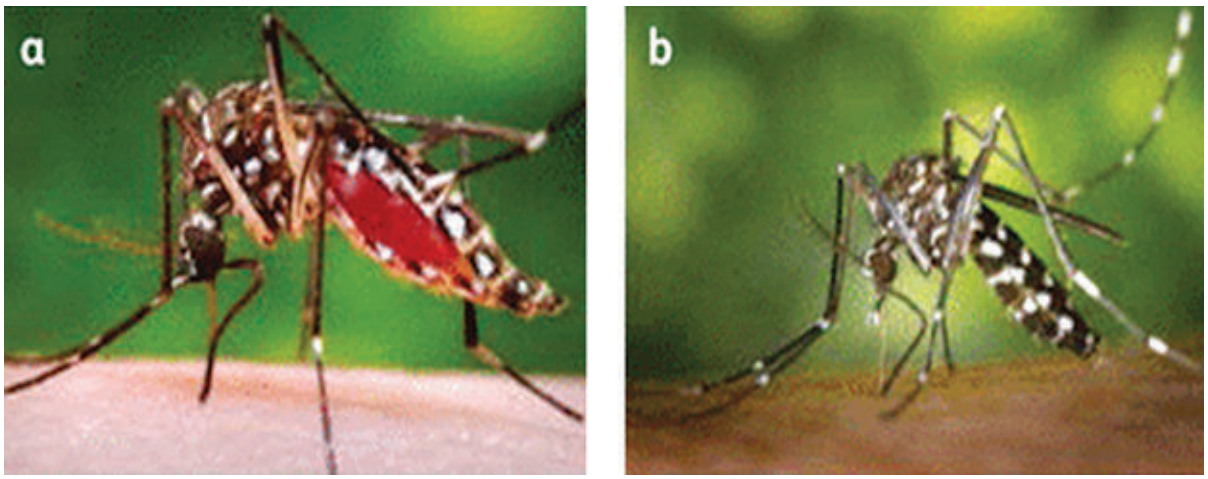

Fig.-4: *a) Aedes aegypti mosquito b) Aedes albopictus mosquito*

[Courtesy by Centers for Emerging and Zoonotic Infectious Diseases (NCEZID)]

Three types of transmission cycle have been described with regard to DENV.

Forest/ Enzoonotic cycle - *Aedes* mosquitos and low primates in the rain forests.

Rural/ Endemic cycle - In small villages or islands where transmission is contained. Virus disappears with developing herd immunity over time.

Urban / epidemic/endemic cycle - in large urban areas in the tropics, periodic epidemics with multiple serotypes.

After a bite from an infected mosquito, initial viral replication occurs in subdermal Langerhans dendritic cells and then the virus migrates to regional lymph nodes. Viraemia occurs through circulating monocytes and macrophages and infects the solid organs and bone marrow.[3]

Clinical feature:

Undifferentiated fever

This stage is seen mostly in the primary infection but may also occur following the initial secondary infection. Clinically, it is difficult to differentiate from numerous other viral diseases and often remains undiagnosed.

Dengue fever [DF]

Dengue fever follows both primary and secondary infections, and is most frequently encountered in adults and older children. Onset of symptoms is characterized by a biphasic, high-grade fever lasting for 3 days to 1 week. Severe headache (mainly retrobulbar), lassitude, myalgia and painful joint, metallic taste, apetite loss, diarrhea, vomiting, and stomachache are the other reported manifestations. Dengue is also known as breakbone fever because of the associated myalgia and pain in joints. Of patients with DF, 50–82% report with a peculiar cutaneous rash. The initial rash is the result of capillary dilatation, and presents as a transient facial flushing erythema, typically occuring before or during the first 1–2 days of fever. The second rash is seen at 3 days to 1 week following the fever, and presents as a asymptomatic maculopapular or morbilliform eruption. Sometimes, individual lesions may merge and present as widespread confluent erythematous areas with pinpoint bleeding spots and rounded islands of sparing, giving a typical appearance of "white islands in a sea of red."[23,25] The cutaneous rash is usually asymptomatic, and pruritis is reported only in 16-27% cases.[9,26] Bleeding episodes are infrequently seen in DF, although epistaxis and gingival bleeding, substantial menstruation, petechiae/purpura, and gastrointestinal tract (GIT) hemorrhage can occur.[20,27]

Dengue hemorrhagic fever [DHF]:

DHF is frequently seen during a secondary dengue infection. However, in infants it may also occur during a primary infection due to maternally attained dengue antibodies. The proposed (National institute of communicable disease) diagnostic criteria for DHF include:

Clinical parameters: Acute-onset febrile phase – high-grade fever lasting from 2 days to 1 week. Hemorrhagic episodes (at least one of the following forms): Petechiae, purpura, ecchymosis, epistaxis, gingival and mucosal bleeding, GIT or injection site, hematemesis and/or malena, Positive tourniquet and hepatomegaly.

Laboratory parameters: Thrombocytopenia (platelet count <100,000/cu mm)

Dengue shock syndrome [DSS]

DSS is defined as DHF accompanied by a unstable pulse, narrow pulse pressure (<20 mmHg), restlessness, cold, clammy skin, and circum oral cyanosis. Progressively worsening shock, multi organ damage, and disseminated intravascular coagulation account for a high mortality rate associated with DSS. The shock persists for a short span of time and the patient promptly recovers with supportive therapy.

Thrombocytopenia is a very common feature in dengue and there is abnormal platelet function. Mild prolongation of prothrombin and partial thromboplastin times with reduced fibrinogen levels is common, but fibrin degradation products have not been found to be elevated to a degree consistent with classic disseminated intravascular coagulation (DIC). Patients with DSS have significant abnormalities in all the major pathways of the coagulation cascade.

[Courtesy: Comprehensive guidelines for prevention and control of dengue and dengue haemorrhagic fever. Revised and expanded edition. (SEARO Technical Publication Series No 60), 2011.11 DF, dengue fever; DHF, dengue haemorrhagic fever.]

Laboratory diagnosis:

One of the more traditional diagnostic methods for the detection of DENV is the virus isolation from samples

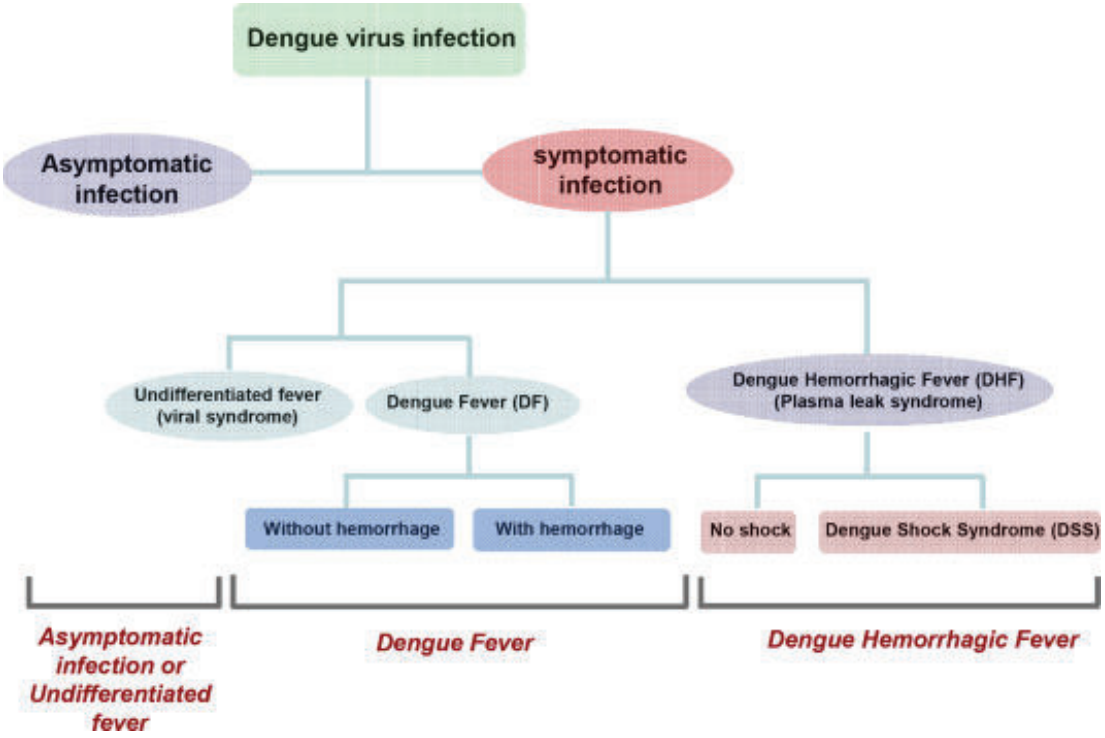

Fig.-5: *Natural course of dengue infection*

obtained from suspected DENV infected patients and cultured in multiple cell lines, such as mosquito cells (C6/36) and mammal cells (Vero, BHK-21 and LLC-MK2) or in live mosquitoes. Despite being definitive, virus isolation for DENV detection is not practical, as it can take several days to perform.[1]

The PCR-based technique has some major advantages as it is fast, specific and sensitive. However, the utilization of PCR-based method may not always be an option, especially in developing countries or counties with lack of resources. Another approach for DENV diagnosis that was first described in 2000 is detecting NS1 in the blood of patients by utilizing an antigen-capture ELISA.[1]

Some serological diagnosis available include Western blotting, plaque reduction neutralization tests, indirect immunofluorescent antibody tests, IgM and IgG antibody-capture ELISAs and hemagglutination inhibition assay (HI) as the more useful diagnostic tests. Detection of IgM can be as early as 3–5 days after infection and remain at detectable levels for several months. On the other hand, IgG appears later during the primary infection, and with a rapid response in a secondary infection. Moreover, detection of both IgM and IgG levels in the patients' serum assists to distinguish primary or secondary dengue infection. [1]

The combination of detecting NS1 along with detecting IgM and/or IgG has demonstrated a drastic improvement to diagnose dengue. Currently, there are some available commercial kits that take advantage of this approach. Utilizing this combination method, the sensitivity of detection reaches high.

The hybridization probe method detects viral nucleic acids with cloned hybridization probes. Probes with variable specificity ranging from dengue complex to serotype specific can be constructed depending on the genome sequences used. The method is rapid and relatively simple and can be used on human clinical samples as well as fixed autopsy tissues. Preliminary data suggest that this method is less sensitive than RT-PCR, but like PCR, the outcome of the test is not influenced by the presence of neutralizing antibodies or other inhibitory substances.[1]

A major problem in dengue laboratory diagnosis has been confirmation of fatal cases. In most instances, only a single serum sample is obtained and serologic testing

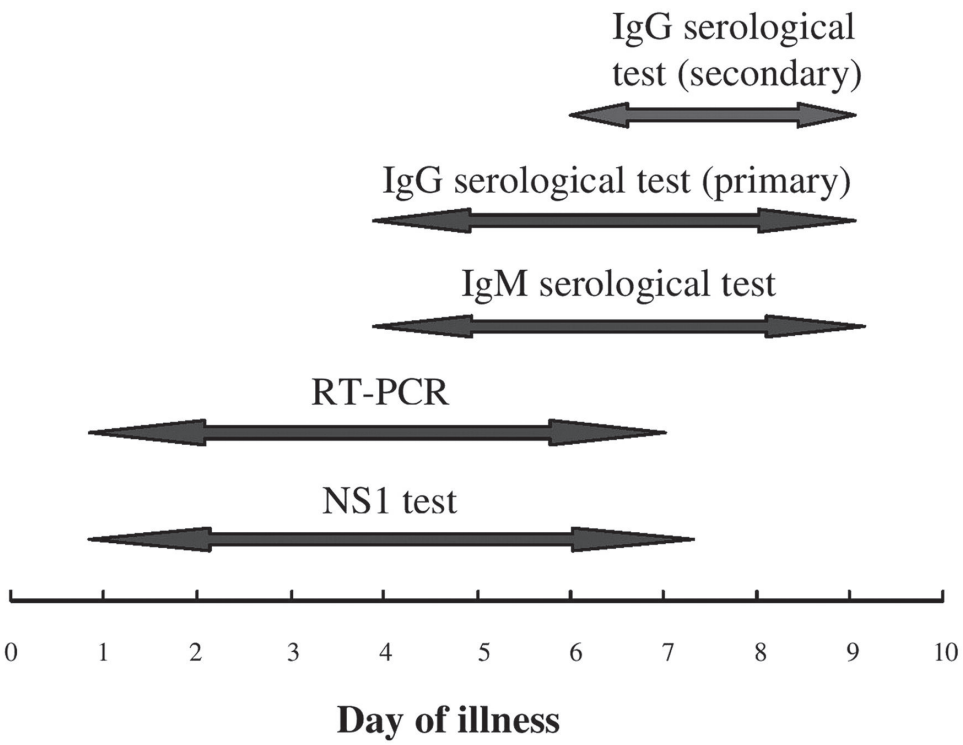

Fig.-6: *Dengue serological test along with the day of illness*

is therefore of limited value. Also, most patients die at the time of or slightly after defervescence, when virus isolation is difficult. With new methods of immunohistochemistry, it is now possible to detect dengue viral antigen in a variety of tissues .Although immunofluorescence tests were used in the past, newer methods involving enzyme conjugates such as peroxidase and phosphatase in conjunction with either polyclonal or monoclonal antibodies are greatly improved. Because tissues can be fresh or fixed, autopsies should be performed in all cases of suspected DHF with a fatal outcome[1].

For dengue test, both government hospitals and private hospitals in Bangladesh have the facility to do the dengue test with reasonable cost. PCR test is recommended for dengue detection in the first seven days after symptom begins. Complete blood count also can be done to look for low platelet count typical of the later stage of the illness and to detect the decrease in hemoglobin, hematocrit and red blood cell (RBC) count that would occur with blood loss associated with severe dengue fever. A positive NS1 test result confirms dengue virus infection without providing serotype information. A negative NS1 test result does not rule out infection. People with negative NS1 results should be tested for the presence of dengue IgM antibody which will determine possible recent dengue infection occur within the past 2 to 3 month.

Discussion:

Dengue is a public health problem in many tropical and subtropical countries, particularly in urban and semi-urban areas. Dhaka City remains the hotspot for the upsurge in dengue cases across the country, the city corporations of Dhaka such as Dhaka North City Corporation (DNCC) and Dhaka South City Corporation (DSCC) should make efforts to involve its residents in community-based programs for elimination of mosquitoes to control dengue outbreaks. Moreover, in Bangladesh, dengue cases are recorded only by the passive surveillance of the disease where only hospitalized patients are officially counted and notified which might impede the dengue control program in Bangladesh because of underestimation of the true dengue burden in Bangladesh. Many asymptomatic or

mild cases of dengue are not hospitalized and remain uncounted. Compared to previous years, in the year 2023, the dengue-related deaths were observed to be the highest in number. In addition in the month of July' 2023; 63% of case and 62% of the deaths were reported from dengue from Directorate general of health services (DGHS).They also has reported 237,251 hospitalizations and 1158 deaths in Bangladesh up to September 2023 due to disease outbreak.

The climate conditions in Bangladesh are becoming increasingly favorable for the transmission of vector-borne disease such as dengue [4]. The peak of the dengue epidemic period is around June to August during the rainy season. It is believed that climate is an important factor for dengue transmission. A previous study analyzed 40,476 cases between 2000 and 2017, and observed that 49.73% of cases were reported during the monsoon season (May–August) and 49.22% during the post-monsoon season (September–December) .Some risk factors affecting dengue outbreaks in Dhaka, including storage of water in household utilities and poor water management, which could be used as mosquito development sites were identified. A recent year-round surveillance study found that the abundance of *Aedes* mosquito larvae in Dhaka varied in different months, and the highest and lowest number of *Aedes* larvae was found in the months of June and February, respectively. A recent study estimated that 24% of the Bangladesh population has been infected by dengue in their lifetime.[9]

To remain consistent with the reviewed publications, we use WHO 1997 criteria in this paper. Manifestations of DENV infection can range from mild-acute undifferentiated febrile illness to classical dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS) according to WHO 1997 dengue guideline. [1]DF is an acute febrile illness that presents symptoms such as bone or joint and muscular pains,

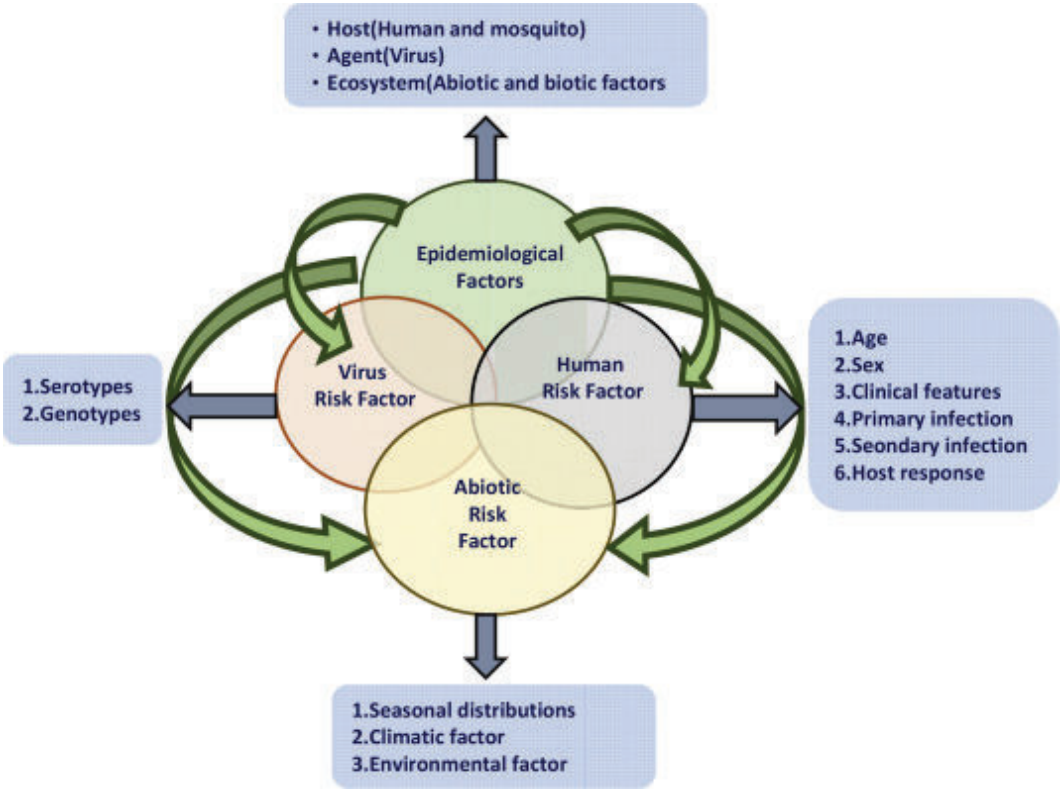

Fig.-7: *Major risk factors of Dengue virus outbreak (Courtesy: Journal of Tropical Medicine and Infectious Disease)*

headaches, leukopenia and rash. DHF has four major clinical manifestations: severe fever, hemorrhage, often with hepatomegaly and in severe cases, circulatory failure. Some of the infected individuals may develop hypovolemic shock which is a result of severe plasma leakage .Bangladesh experienced the largest dengue outbreak in 2019. Abdominal pain, vomiting, and diarrhea were also reported as common manifestations of dengue infection in the non-endemic zone of Bangladesh [39]. The incidence of bleeding manifestations was low (about 5%) in the 2019 outbreak. The most common bleeding manifestations were melena (5%) and gum bleeding (3%) [40]. Notably, DSS was reported in up to 10% of cases compared to only 0.6% in the first outbreak. Besides, hypotension, a feature of plasma leakage and impending shock, was recorded in about one-fourth of the cases in the 2019 outbreak [29]. Other signs of plasma leakage, including edema, and ascites, pleural effusion, were also noted. On the other hand, signs of shock were recorded only in 11% of cases in a study conducted among pediatric patients between 2006 and 2008 [38]. Therefore, it is discernible that dengue is possibly going through an epidemiological shift towards more severe disease (i.e., DSS rather than DHF) in Bangladesh. The resurgence of the DENV-3 serotype could be a possible driver for such change [41]. In addition, it is important to note that WHO updated the case definition of severe dengue in 2009. Compared to the 1997 classification system, the 2009 classification is more sensitive in detecting severe dengue cases, especially cases with DSS. The revised case definition could partly contribute to the higher prevalence of severe cases observed in recent outbreaks. Nonetheless, this is alarming for Bangladesh as future outbreaks could be devastating and claim more lives.

Microbiological laboratory testing confirms the diagnosis of DF. Virus segregation in cell cultures, nucleic acid demonstration by polymerase chain reaction (PCR), and serological detection of viral antigens (such as NS1) or particular antibodies are the preferred microbiological assays.[42] Viral segregation and nucleic acid demonstration provide precise diagnosis, although the high cost limits the availability of these tests.

Although the DNCC and DSCC have adopted several initiatives such as the opening of control rooms for conducting special anti-mosquito combing operations, including awareness building programs among residents, strengthening dengue surveillance programs to destroy the breeding sites of *Aedes* mosquitoes, and providing free dengue tests and advice the vector control program needs to be further enhanced for effective vector control, as the dengue cases are still on the increase. Although previous dengue outbreaks (from 2018 to 2020) were mainly centered in Dhaka, the 2019 and current 2023 outbreaks spread across the country, including all divisional cities. This year, the upsurge in cases started earlier (around the last week of April) compared to previous years. As of 27 August 2023, a total of 1,19,133 cases and 569 deaths have been reported from all the district of the country .Therefore, the country should remain prepared for an immediate response with an improved, rapid diagnostic and continuous monitoring system, which is likely to limit the spread and impact of the infection. Moreover, an early detection of disease progression associated with severe dengue is important for proper medical care, which may reduce fatality rates from severe dengue infection.

Conclusion:

Dengue has evolved as a global life-threatening public health concern, affecting around 2.5 billion individuals in more than 100 countries. Dengue is now one of the most common reasons for hospital admission in Bangladesh during the rainy seasons. The mortality rate for admitted patients gradually becomes high which is alarming. The most important clinical feature of dengue is increased vascular permeability leading to DSS. Infants and younger people are particularly prone to the development of shock and adults are at increased risk of bleeding. The physician should be aware about the varied clinical manifestations of this condition and ensure an early and adequate treatment plan. Future directions to combat this dreadful disease aim at methods of mosquito control, development of vaccine, and antiviral drug. Therefore, a sustained and strengthened surveillance system is essential for the early detection and isolation of DENV-infected patients to limit the spread of the infection.

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