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Dengue virus: epidemiology, molecular pathogenesis, risk factors, and public health challenges in endemic regions

Abstract

Dengue virus (DENV) is a major global health concern, particularly in tropical and subtropical regions where Aedes aegypti and Aedes albopictus mosquitoes serve as primary vectors. This single-stranded RNA virus belongs to the Flaviviridae family and exists in four serotypes (DENV-1 to DENV-4), each capable of causing mild to severe illness, including Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS). The increasing incidence of dengue, driven by urbanization, climate change, and inadequate vector control measures, presents significant public health challenges. Molecular epidemiology plays a crucial role in understanding viral evolution and transmission dynamics, while diagnostic techniques such as ELISA and PCR improve early detection. Pregnant women are particularly vulnerable, with DENV infections linked to adverse pregnancy outcomes, including stillbirth and low birth weight. Additionally, socio-demographic and environmental factors, such as poor sanitation and unplanned urbanization, exacerbate dengue transmission, especially in low-income communities. In Nigeria and West Africa, dengue remains underdiagnosed and frequently misclassified as other febrile illnesses, such as malaria, further complicating surveillance efforts. Laboratory diagnostic limitations, including cross-reactivity with other flaviviruses, hinder effective disease management. Preventive measures primarily focus on vector control, but these efforts are often costly and insufficient. Ongoing research into vaccine development and antiviral therapies offers hope for future control strategies. However, the complexity of DENV's immune interactions and co-circulating serotypes presents challenges in vaccine design. Strengthening public health infrastructure, improving diagnostic capacity, and increasing community awareness are essential for mitigating dengue's impact and preventing future outbreaks.

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Introduction

With mosquito-borne illnesses like dengue, West Nile, chikungunya, and Zika viruses becoming more common, infectious diseases have had a major impact on world health. Aedes aegypti and Aedes albopictus mosquitoes are the main vectors of the dengue virus, a single-stranded RNA virus belonging to the Flaviviridae family.[1] All four serotypes of the virus—DENV-1, DENV-2, DENV-3, and DENV-4—may result in dengue fever, which can range in severity from mild to severe hemorrhagic symptoms. In the study of Chee et al., adult patients with fever who had no other diagnosis than dengue were recruited and used the World Health Organization's (WHO) 2009 definitions for dengue hemorrhagic fever (DHF) and severe dengue (SD) were both used to define the results. In 469 dengue-confirmed patients, the infecting serotype was found to be 22.0% dengue virus serotype 1 (DENV-1), 57.1% DENV-2, 17.1% DENV-3, and 3.8% DENV-4. While DENV-2 cases were linked to joint discomfort and a decreased platelet count, DENV-1 cases were more likely to present with red eyes.

In a related study, Rabaa et al.,[2] reported that infection with secondary DENV-2 is more likely to cause severe illness than other serotypes, according to earlier studies of dengue in children.[3] Primary DENV-1 instances, on the other hand, were more obvious, whereas primary DENV-2 and DENV-3 cases were typically quiet.[4]

Additionally, phylogenetic data that has been published indicates that the Asian genotype of DENV-2 is more common in these investigations than the Cosmopolitan genotype that is circulating in Singapore, which has an unknown effect on disease manifestation.[2]

According to phylogenetic analyses of the DENV envelope protein gene, there is significant variation even among DENV serotypes, leading to different genotypes with different potential for epidemics.[5] Variations at the serotype and molecular level are significant for both dengue endemic and non-endemic countries when it comes to treating feverish returned travelers infected with different dengue viruses that are spreading around the world.

The transmission of the dengue virus has been reported to occur in several routes.[4] Although mosquito bites are the main way that DENV is spread, direct blood contact—such as during organ transplants and transfusions—can also happen. According to the World Health Organization (WHO), the disease is a major worldwide health concern that primarily affects tropical and subtropical climates. Controlling its spread is made more difficult by the lack of licensed antiviral medications and vaccinations.[6,7]

With an estimated 390 million cases yearly, dengue virus infections have tripled in the past 50 years. Vector proliferation has been made easier by rapid urbanization, population increase, and climate change, especially in underdeveloped areas with inadequate sanitation. Women who are pregnant are especially at risk, as infections can result in issues such as maternal hemorrhage, premature birth, stillbirth, and low birth weight in the fetus. Genetic predisposition, demographic status, and socioeconomic factors all affect an individual's vulnerability to infection.

One of the main vectors of DENV is the Aedes mosquito. The extremely anthropophilic species Aedes aegypti lays its eggs in water-holding containers and flourishes in urban settings. It takes 8–12 days for the virus to incubate in the mosquito before it may spread to a

new host. Notably, Aedes populations can persist in some areas due to the presence of desiccation-resistant eggs, which keeps the virus endemic.

To comprehend the evolution and transmission of DENV, molecular epidemiology is essential. Early detection has been enhanced by diagnostic techniques including enzyme-linked immunosorbent test (ELISA) and polymerase chain reaction (PCR). Outbreak prediction and control efforts are improved by epidemiological surveillance using genome sequencing, population mobility studies, and geographical mapping.[8]

DENV infection during pregnancy increases the chance of serious consequences, such as difficulties for both the mother and the fetus. Pregnant women are more vulnerable to infections due to their compromised immune systems, and vertical transfer to the fetus is still a possible risk.[9] According to studies, pregnant women in endemic areas require focused interventions because DENV-2 infections are more severe than those caused by other serotypes.[10,11]

By changing the distribution of mosquito habitats, climate change has had a major impact on DENV transmission. The perfect environment for vector reproduction is created by rising temperatures, more precipitation, and higher humidity, which increases the persistence and transmission of viruses. Higher infection rates are found in densely populated areas as a result of urbanization's further facilitation of Aedes mosquito growth.[12]

Vector control techniques, such as insecticide-treated nets, biological control, and environmental sanitation, are essential to the fight against dengue. To reduce the transmission of disease, public health programs emphasizing early detection and community awareness are essential.[13-15] Prospects for managing dengue in the future are bright thanks to ongoing research into vaccine development and antiviral treatments. Furthermore, developments in genetic epidemiology and bioinformatics provide fresh perspectives on viral evolution and epidemic forecasting.[16]

Arboviruses

Arboviruses are distinct from other animal viruses in that they spread to vertebrates through a process known as biological transmission, which is carried out by blood-sucking arthropods (vectors). Numerous medical entomologists, epidemiologists, and virologists have been fascinated by this unusual mode of transmission that involves the three essential components (virus, vector, and vertebrate). It has also sparked important discussions about everything from the benefits of such a complex mode of transmission to its effects on virus genetics.[17]

The sharp rise in the prevalence and severity of both established and newly discovered arboviral illness issues has demonstrated the significance of arboviral infections.[18-20] In the United States alone, 9,858 confirmed cases and 262 fatalities were reported in 2003 as part of the ongoing West Nile fever outbreak in North America. In Asia, Japanese encephalitis is thought to cause between 30,000 and 50,000 cases per year, with 10,000 fatalities. In addition, almost 50 million people globally contract dengue each year.[13]

Arbovirus transmission has become a fundamental aspect of research and discussion across diverse disciplines, including disease-specific investigations, epidemiology, vector control, virology, host-pathogen interactions, and ecological dynamics.[21] Because arboviral research encompasses several significant scientific domains, it has proven difficult to organize and compile the data and observations of biological transmission reported in different disciplines.[22,23]

Dengue virus (DENV)

The dengue virus is a capsid-enclosed, single-stranded, positive-sense RNA flavivirus that is surrounded by an envelope protein made up of the structural proteins prM/M (pre-membrane/membrane) and E (envelope). NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5 are examples of nonstructural proteins (NS) in DENV (Martins et al., 2012). During the viral replication cycle, both structural and nonstructural proteins are translated and transcribed, allowing intracellular antigen processing mechanisms to use them. The roles of these NS proteins vary. For example, NS3 carries out helicase and protease activities, while NS1 collaborates with NS4A/B to encourage viral replication. While NS4B encourages the NS3 helicase to separate from viral RNA, NS4A triggers autophagy.[19]

As an RNA-dependent RNA polymerase that duplicates the viral RNA and an RNA methyltransferase enzyme that enables polyprotein translation while protecting the viral genome through RNA capping, NS5B continues to be the largest and most conserved DENV protein. Targeting NS5 for vaccine development and antiviral treatments is receiving a lot of attention because it is essential for viral replication and a primary target for cytotoxic T-cell responses.

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By attaching to the transmembrane and CARD-like domains of the mitochondrial antiviral signaling protein (MAVS), NS4A is also linked to the suppression of RIG-I interaction with MAVS. By preventing the phosphorylation of TANK binding kinase1 (TBK1) and interferon regulatory factors (IRFs), NS2A and NS4B also contribute to limiting the RIG-I/MAVS signaling pathway and preventing the induction of IFN. By cleaving the protein that stimulates the interferon gene, NS2B/3 prevents the synthesis of interferon. DENV-1, 2, 3, and 4 are the four main serotypes.

When a female Aedes mosquito—primarily *Aedes aegypti* and, less commonly, the cold-adapted *Aedes albopictus*—bites a person, it can transmit the dengue virus (DENV). A first infection with any of the four DENV serotypes triggers a cross-reactive immune response that provides only partial and short-lived protection against the other serotypes. This cross-reactive immunological memory eventually wanes over time. If a person is infected again with the same serotype after this memory has diminiÍÍÍÍshed, a more effective and protective immune response can be mounted. According to McCarthy, recurrent infection with distinct serotypes is linked to severe clinical manifestations and has significant consequences, such as the potential for death.

It is difficult to design a DENV vaccination that is extremely effective against all four serotypes. However, a large population of previously infected persons can become protected significantly because of herd immunity. Infection with a specific dengue virus (DENV) serotype typically confers long-lasting, possibly lifelong, homologous immunity. However, cross-protective (heterotypic) immunity against other DENV serotypes is transient, generally lasting less than 1 to 3 years. This immunological profile underlies the characteristic cyclical epidemiology of dengue virus transmission. Following an epidemic dominated by a particular serotype, population-level immunity rises, temporarily suppressing transmission through herd immunity effects.

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This results in a period of reduced incidence—an interepidemic phase—that typically lasts 3 to 5 years. As heterotypic immunity wanes and a different DENV serotype is introduced or re-emerges in the population, conditions become favourable for a new epidemic. This pattern of serotype-driven cyclicity has been consistently observed across dengue-endemic regions.[21,24]

Herd immunity in human populations plays a critical role in shaping both the transmission dynamics and outbreak potential of arboviruses. When a virus is introduced into a population with little or no prior immunity, large-scale, explosive outbreaks can occur. In contrast, once herd immunity reaches a threshold that limits efficient transmission, only smaller, sporadic outbreaks may occur—or transmission may cease entirely. The overall influence of herd immunity on arbovirus circulation, whether in enzootic or endemic/epidemic settings, varies substantially depending on the lifespan and turnover rates of the primary amplification hosts.[24]

Since all four of the DENV serotypes can co-circulate in the same nation, secondary infections are widespread in many regions of the world that have become hyperendemic. In addition to the 30% polyprotein divergence across the four DENV serotypes 1-4, each serotype is made up of phylogenetically separate "subtypes" or "genotypes" with varying geographic distributions.

Measures for prevention

In the ongoing quest for a vaccine and anti-dengue medications, two strategies to stop the spread of DENV are lowering the number of vectors and teaching residents in impacted areas about fundamental safety precautions. Programs for preventing vectors include strict surveillance, the use of insecticides and genetically engineered mosquitoes, the reduction of possible breeding grounds, and the encouragement of quality infrastructure and housing.

Recent advances in genetic control technologies have led to the development of engineered mosquitoes aimed at either reducing mosquito populations or altering them to prevent disease transmission. Suppression approaches include the Sterile Insect Technique (SIT), Incompatible Insect Technique (IIT), and gene drive systems, which all reduce the number of viable offspring in wild populations. In contrast, population modification strategies involve releasing genetically modified mosquitoes that carry traits—such as resistance to specific pathogens—which can spread through natural mating, reducing the mosquitoes' ability to transmit diseases.[25]

Suppression strategies help mitigate environmental concerns, such as soil or water contamination, and avoid health risks associated with pesticide exposure. Another important benefit of population suppression methods is their ability to address the growing problem of insecticide resistance. By offering an alternative mechanism of control, these technologies can reduce reliance on chemical interventions and help preserve the efficacy of existing insecticides. Furthermore, some genetic tools, such as gene drive systems, have the potential to spread traits through mosquito populations more rapidly than would occur under normal inheritance. This can result in a swift and sustained reduction in mosquito numbers, especially in areas where traditional control methods have been less effective.[25]

Population modification strategies aim to alter mosquitoes so that they cannot transmit pathogens, rather than reducing their numbers. This is achieved by introducing genetic modifications that make mosquitoes refractory, or resistant, to infections such as malaria or dengue. One of the primary advantages of this approach is its direct targeting of disease transmission, which can significantly reduce the incidence of infection in human populations without eliminating the mosquito species itself.[25]

Individuals can protect themselves by using personal protection. Protective clothes and pesticide sprays are examples of personal protection. Inadequate water supply and sewerage systems, along with the unplanned, fast expansion of urban centers in Southeast Asian and South American nations, have a significant impact on DENV transmission.

Socio-demographic and environmental determinants DEN-V

Arboviral illnesses have been linked to a variety of causes. Sociodemographic variables and the features of the home and its environment are the most crucial.[19] Research has indicated that those in vulnerable socioeconomic circumstances are more susceptible to DENV and CHIKV; yet other research has found that ZIKV and DENV have the reverse effects.[19] Low socioeconomic level individuals sometimes live in filthy conditions, which can lead to a rise in mosquito populations and, thus, a greater risk of contracting these illnesses.

Many local factors, such as vegetation cover, can prevent disease transmission; however, a number of studies failed to establish a connection between disease transmission and vector abundance.[19] Vectors are frequently seen inside private residences and are more common in urban areas. Residence is probably used as a proxy for infection sites in most studies. However, studies have shown that vectors prefer to feed during the day when most people are at work or, in the case of kids and teens, at school. The finding of Ae. aegypti in schools that tested positive for DENV and ZIKV supports this theory, identifying schools as one of the likely locations of transmission.

Risk factors for severe dengue

To comprehend the intricate interaction of host and viral variables, DENV pathogenesis is still a difficult jigsaw puzzle with many missing pieces. Despite extensive research, little is known about it. Numerous risk variables, including age, the host's genetic background, the virus serotype and genotype, and secondary DENV infection by a heterologous serotype, influence the severity of DENV infection. Lastly, the genotype and serotype of the virus also affect the disease's symptoms and course. Although epidemiological evidence served as the initial basis for these observations, growing laboratory and experimental data have helped to identify DENV virulence as a significant risk factor.

Host genetics

The host's genetic background, which includes a variety of polymorphisms, may have significant effects on disease susceptibility in addition to the influence of viral genetic determinants. A genome-wide approach to the study of host genetic susceptibility has been made possible by advancements in high-throughput genotyping of genetic variants. Functional trials to try and connect genetic connection with any process in disease etiology have not been done in the majority of studies.

Cuban dengue outbreaks have provided indirect proof of the host's genetic significance, as individuals with African heritage were found to have a lower risk of DHF/DSS than those with European ancestry. The decreased vulnerability to DHF seen in Black Caribbean and African populations aligns with the data made in Cuba. Interestingly, there are few occasional reports of DHF patients even though DENV is present in 19 African nations.

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Host health and age

There is a higher correlation between severe dengue and sickle cell anemia, peptic ulcers, diabetes mellitus, and bronchial asthm). However, further research is required to determine how dengue affects other infections and chronic illnesses. In contrast to secondary infections, which frequently result in severe dengue, primary infections are thought to cause mild illness in children. The majority of cases of DHF/DSS in Southeast Asia occur in children. It is thought that children's naturally more permeable vascular endothelium accounts for the higher relative frequency of DSS in children compared to adults. There isn't a clear consensus; research from South American nations has shown that adults are the most affected, with similar and conflicting findings.

Dengue virus in Nigeria and West Africa

Nigeria has a high prevalence of arboviruses because the mosquito vectors that spread dengue, yellow fever, chikungunya, and malaria (*Aedes* spp.) are well-established there. Accordingly, it is not unusual for dengue to co-infect with other arbovirus illnesses; in Nigeria, this has been show). These co-infections may offer a chance for genetic material and mutations to be exchanged, leading to the formation of more fit strains with more severe illness. Accurate serological diagnosis may also be impacted by antibody cross-reactivity by viruses belonging to the flaviviridae family.[13] Early dengue symptoms might be mistaken for those of other tropical illness fevers, such as typhoid and malaria.

The majority of febrile sickness cases in Nigeria, where malaria is widely endemic, are probably treated as presumed malaria. In Ibadan, Nigeria, we recently found that 10% of individuals with malaria also had an active dengue infection. All of the malaria patients in the study tested positive for dengue IgG antibodies, indicating a history of dengue infection and in line with the dengue virus's endemicity in the area, according to additional analysis of dengue IgG seroprevalence among malaria patients.[26]

Dengue fever may be the most common cause of unclassified febrile diseases in Nigeria, where it is endemic in practically every state.[12] Both urban and rural areas are affected by dengue fever, however, in the past, more cases were documented in urban areas than in rural ones. Because dengue fever is not a public health priority, surveillance for it is inadequate in Nigeria. As demonstrated by the underdiagnosis and incorrect diagnosis of viral infection in numerous unclassified febrile illnesses, it is therefore linked to a lack of public awareness of the virus and inadequate comprehension by medical professionals. Nigeria's dengue disease burden may be greatly underestimated.

Following an outbreak in Durban, South Africa, in 1926, clinical reports of dengue fever were first made in Africa. But it wasn't until the 1960s and 1970s that the dengue virus was isolated from human sera in West Africa. In particular, the dengue virus was initially discovered in 1960 in Ibadan, Western Nigeria. Even though there have been numerous reports of isolated dengue infection outbreaks in Nigeria since 1960, many of these outbreaks were likely overlooked, underreported, or not recognized because medical personnel were unaware of them and diagnostic tools were unavailable in medical facilities.[6]

According to recent reports, dengue viruses are a substantial contributor to acute fevers in Nigeria. In Maiduguri, in Northern Nigeria, and Ilorin, in Western Nigeria, recent seroprevalence studies revealed that 10.1% and 30.8% of participants, respectively, were seropositive for dengue subtype-3 virus (DENV-3), underscoring the growing significance of dengue in Niger. In South-Western Nigeria, dengue IgM seroprevalence among children with fever has also been reported to be 17.2% and 30.8%, respectively.[6,13] These high prevalence rates of dengue IgM antibodies and symptomatic dengue virus infections suggest that dengue may be endemic and that many illnesses may have gone unnoticed by frontline healthcare providers. High vector densities have also been observed in densely populated Nigerian cities. Together, these results point to dengue as a developing public health issue in Nigeria, the scope of which need more clarification.

Evidence of high incidence of dengue and malaria co-infection in Nigeria makes diagnosing dengue even more difficult. According to a recent study, 10% of confirmed cases of malaria in Ibadan, South-Western Nigeria, also had active dengue co-infection. All of the malaria patients in the study tested positive for dengue IgG, indicating a history of dengue infection and being in line with the dengue virus's endemicity in this region, according to additional analysis of dengue IgG seroprevalence among malaria patients. The Anopheles mosquito, which spreads malaria, and the Aedes aegypti mosquito, which spreads dengue, yellow fever (YFV), and chikungunya, are both highly prevalent in Nigeria.[26]

Potential risks to public health

Unplanned urbanization, inadequate monitoring and vector management, poor public health, international travel, and virus and vector development are some of the reasons why there have been more documented dengue cases since the 1980s. Comprehending infection risk variables is crucial for public health management initiatives.[17] For example, it has proven challenging to assess the differences in infection rates between males and females. Males had a twofold higher risk of infection than females, according to three separate studies based on dengue outbreaks in Singapore and India. Both sexes are equally impacted, according to a few South American research, including our most recent one in Nigeria.[14]

All things considered, a thorough assessment of the disparities in infection rates across sexes necessitates carefully planned research that takes into account the biological and social elements that contribute to dengue transmission in the community. Incidence and, in particular, dengue epidemics have been prevalent during the rainy season, and the role of climate change in DENV transmission has been studied earlier. The transmission of DENVs is accelerated when the mosquito vector has access to suitable breeding grounds. During the wet season, mosquito densities increase due to the need for water for reproduction, which raises the number of dengue cases during this time.[26]

The majority of Nigerian cities have stagnant water bodies and water accumulates in waste metal containers and car tires due to inadequate garbage disposal and poor drainage systems. The mosquito vectors, which are how DENV is spread, breed in these media. The danger of human-mosquito transmission is also increased in these places due to the rise of vulnerable individuals, and vice versa. Consequently, because of the nature of the infection route, people who often come into contact with the mosquito vector are most at risk of contracting the disease.

Limitations of laboratory diagnosis

The absence of standard laboratory diagnosis affects dengue surveillance in Nigeria. Dengue can be diagnosed in a lab setting using serological assays, polymerase chain reaction (PCR), and culture. Each test has limits, though, and the detection targets many virological indicators, such as the infectious virus in culture, the

viral RNA in PCR, and the DENV-specific antibodies (IgG/IgM) or antigens in serology.

Using particular cell lines, DENV can be separated from serum, plasma, or washed buffy coat. It is also possible to use autopsy tissues from dead cases, particularly the thymus, liver, spleen, and lymph nodes. Acute patient samples with a high enough viral load are necessary for virus culture. Consequently, there is a limited window of time during which DENV can be effectively isolated from patient serum. Since viremia peaks before symptoms appear, if a patient seeks medical attention, their virus levels may drastically decline.[9]

Additionally, a day or two after the fever has subsided, increasing antibody levels disrupt virus culture. The application of this approach is restricted by several practical factors in addition to sample-gathering constraints. The virus's culture takes a lot of time and effort, thus enhanced laboratory safety capabilities, like bio-safety level 3, are required. As a result, people must receive professional training. The regular use of this diagnostic tool is restricted by these restrictions, particularly in underdeveloped nations.[9]

PCR uses oligonucleotide primers unique to DENV to detect viral RNA from serum, plasma, or cells. However, because most dengue-prone or endemic nations lack the capacity for routine molecular diagnostics, this method is monetarily prohibitive. A straightforward and affordable method based on the existence of anti-DENV antibodies is frequently employed. The screening of dengue IgG/IgM antibodies is the foundation of this technique. After infection, the acute anti-DENV IgM antibody response lasts for a few weeks, but the IgG antibody response lasts for years.[10,27]

It has been proposed that seroconversion after IgM generation takes place 4–8 days after fever onset. This approach is constrained by the significant possibility of false-negative results because of a prolonged seroconversion time and false-positive results because of possible cross-reactivity with other flaviviruses, such as immunization against the yellow fever virus.[8]

Due to the severe limitations of these techniques, the identification of the viral NS1 protein has become a viable substitute for serology, PCR, and culture. Shortly after contracting dengue, the NS1 protein, which is generated during viral replication, can be found. That is the period between the onset of fever and nine days after infection, before IgM seroconversion.

Treatment and therapeutic approaches

The only strategy for preventing disease at the moment is vector control, which is seen to be both costly and ineffectual. Since there are currently no vaccinations or antiviral medications to prevent DENV infection, supportive care—which includes bed rest, antipyretics, and analgesics—is the mainstay of treatment for dengue patients.[9]

The many phases of the viral replication cycle have been the focus of the development of innovative treatment strategies for dengue sickness. Significant attention has been paid to the E protein's structural alterations and interactions with prM or M. Antiviral agents can target the entrance, assembly, or maturation stages of the virus life cycle during these transition states. Antiviral peptides may be a promising treatment for DENV since they have been developed and tested to block the entry of both DENV and the West Nile virus (WNV) with encouraging results. Since it is much more difficult to get target molecules into the host cell during stages of fusion and maturation, targeting the entry of mature viruses into host cells is a particularly intriguing candidate.[10]

Making peptides that resemble the M protein's pr peptide has been another strategy to stop the structural alterations of the E-prM protein interactions. This stops membrane fusion and the release of freshly created virions. Since most viruses have proteases, which are generally necessary for effective replication, the viral protease is another intriguing target for antiviral discovery. The DENV protease NS2B-NS3 may eventually be inhibited by hepatitis C virus (HCV) protease inhibitors.[27]

Usually, prodrugs and nucleoside analogues must be changed into their antiviral nucleotide metabolite forms. Combined with IFN, ribavirin (1-b-d-ribofuranosyl-1H-1, 2, 4-triazole-3-carboxamide) exhibits broad-spectrum antiviral action to fight HCV infection. Viral and cellular protein capping and polymerase activity are indirectly impacted by ribavirin's depletion of the nucleotide pool. Furthermore, ribavirin makes the replication of several viral genomes more prone to errors. Ribavirin has proven ineffective in animal models and has a cytostatic effect on DENV-infected cells, despite its positive in vivo outcomes with several RNA viruses.

Conclusion

Dengue virus (DENV) remains a significant global health challenge, particularly in tropical and subtropical regions where the Aedes aegypti and Aedes albopictus mosquito populations thrive. The increasing incidence of dengue, driven by urbanization, climate change, and poor vector control, underscores the urgent need for coordinated public health responses. Despite advancements in molecular epidemiology, diagnostic techniques, and potential vaccine development, there are still major gaps in dengue management, especially in regions like Nigeria and West Africa, where underdiagnosis and misclassification of cases persist. The co-circulation of multiple DENV serotypes further complicates disease control, as secondary infections with different serotypes can lead to severe complications such as Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS).

In addition to epidemiological concerns, the article highlights the critical role of socio-demographic and environmental factors in dengue transmission. Poor sanitation, inadequate surveillance, and a lack of awareness among healthcare providers contribute to the underestimation of the dengue disease burden. Furthermore, the complex interactions between host genetics, viral evolution, and immune responses present challenges in developing an effective universal vaccine and antiviral treatment. While vector control remains the primary preventive strategy, it is both expensive and inefficient in the long term. The lack of a standardized laboratory diagnostic system further hinders effective case identification and surveillance, leading to delays in outbreak response and control efforts.

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Conflict of interests

Authors declare no conflict of interest.

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