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Review

Seroprevalence of Dengue Infection in the Caribbean: A Literature Review

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Abstract

The Caribbean exhibits hyperendemic dengue transmission with near-universal adult seroprevalence in many territories, driven by sustained co-circulation of all four DENV serotypes and the domestic ecology of *Aedes aegypti*. Serosurveys report adult IgG rates as high as 93–100% in the French West Indies, Puerto Rico, and Jamaica, while children frequently acquire multitypic immunity before adolescence. High inapparent infection rates and population mobility complicate surveillance and mask true transmission intensity. These immunoepidemiological conditions elevate the risk of severe disease via antibody-dependent enhancement and challenge both acute diagnostics and vaccine policy. Effective control demands year-round integrated vector management, improved molecular and neutralization-based surveillance, pediatric-focused prevention strategies, and cautious deployment of balanced tetravalent vaccines informed by serotype-specific and genomic data.

Keywords: dengue; seroprevalence; Caribbean island; viral genome; *Aedes aegypti*

Introduction

Dengue virus infection presents a substantial global health challenge, particularly in tropical and subtropical regions such as the Caribbean, where environmental conditions facilitate its widespread transmission. Understanding the seroprevalence of dengue in these regions is crucial for assessing population immunity, estimating the force of infection, and informing effective public health interventions [1]. This review synthesizes the current literature on dengue seroprevalence in the Caribbean, highlighting variations across different populations and geographical areas within the region, which is essential given the wide range of reported seroprevalence rates globally [2]. Notably, seroprevalence often demonstrates an age-dependent increase, with all four dengue virus serotypes circulating throughout the region [2,3].

Background of Dengue Fever

Dengue fever, caused by the dengue virus, is a mosquito-borne flavivirus that presents a broad spectrum of clinical manifestations, ranging from asymptomatic infection to severe and potentially fatal Dengue Hemorrhagic Fever and Dengue Shock Syndrome. Dengue virus represents the most significant mosquito-borne viral threat to global public health, with its incidence increasing nearly 30-fold over the past few decades [4,5]. Approximately half of the world's population resides in at-risk areas, leading to an estimated 390 million infections annually, of which approximately 96 million manifest clinically [6,7]. The complexity of DENV pathogenesis stems from the interplay between its four distinct serotypes (DENV-1, -2, -3, and -4) and the human immune system, where subsequent

infections with heterologous serotypes often lead to severe, life-threatening conditions such as Dengue Hemorrhagic Fever and Dengue Shock Syndrome [8–10].

Virology and Genome Architecture

DENV is a member of the *Flavivirus* genus within the *Flaviviridae* family [5,11]. It is characterized by a single-stranded, positive-sense RNA genome of approximately 11 kilobases [5,7]. This genome contains a single open reading frame flanked by 5' and 3' untranslated regions, which are critical for viral replication and host adaptation [12]. The ORF is translated into a single polyprotein that viral and host proteases subsequently cleave into three structural and seven non-structural proteins [11,12].

Structural Proteins

Structural proteins are shown in Table 1.

Table 1. Summary of Structural proteins of Dengue viruses.

Structural Proteins	Functions	Reference
Capsid (C)	Associates with the viral RNA to form the nucleocapsid	[12]
Pre-membrane/Membrane (prM/M)	Acts as a chaperone for the envelope protein, preventing premature fusion during the maturation process in the acidic environment of the Golgi	[12]
Envelope (E)	The primary surface protein responsible for host cell receptor binding and membrane fusion. It is the major target for neutralizing antibodies.	[11,12]

Non-Structural Proteins

Non-structural proteins are shown in Table 2.

Table 2. The non-structural proteins are essential for genome replication and subverting host innate immunity.

Protein	Functions	Reference
NS1	A unique glycoprotein that is both membrane-associated and secreted as a hexameric lipoparticle [12,13]. High circulating levels of NS1 are strongly correlated with severe disease and vascular leakage.	[12]
NS2A and NS2B	NS2B serves as an essential cofactor for the NS3 protease activity.	[11,14]
NS3	A multifunctional protein with protease, helicase, and NTPase activities. It cleaves the viral polyprotein and unwinds RNA during replication.	[11,14]
NS4A and NS4B	These proteins induce host cell membrane remodeling to create replication organelles. NS4A is also implicated in inducing autophagy to promote viral survival.	[11,14,16]
NS5	The largest and most conserved protein, providing RNA-dependent RNA polymerase activity for replication and methyltransferase activity for 5' RNA capping. It also suppresses host interferon signaling by localizing to the nucleus.	[11,14]

Mechanism of Infection and Viral Life Cycle

The DENV replication cycle is a complex, multi-step process that primarily targets cells of the myeloid lineage, including monocytes, macrophages, and dendritic cells [17,18].

Attachment and Entry

Viral entry begins with the E protein binding to various host cell receptors, such as DC-SIGN on dendritic cells, the mannose receptor on macrophages, and heat shock proteins (HSP70/HSP90) [11,17]. Following attachment, the virus is internalized via clathrin-mediated endocytosis [15]. As the endosome acidifies, the E protein undergoes a conformational change from a homodimer to a homotrimer, facilitating the fusion of the viral envelope with the endosomal membrane and releasing the nucleocapsid into the cytoplasm [11].

Translation and Replication

Upon uncoating, host ribosomes directly translate the positive-sense RNA at the endoplasmic reticulum [12]. DENV induces extensive morphological alterations of the ER to form viral replication organelles (vROs), which consist of convoluted membranes and vesicle packets [16]. These specialized compartments provide a scaffold for the replication complex (NS3, NS5, and other NS proteins) and shield double-stranded RNA intermediates from host innate immune sensors [12,16]. The NS5 RdRp synthesizes a negative-sense RNA template, which then serves as a scaffold for the production of numerous positive-sense genomic RNAs [14].

Assembly and Release

Progeny viral genomes are packaged by the C protein and bud into the ER lumen, acquiring an envelope embedded with prM and E proteins [15]. These immature, "spiky" virions transit through the Golgi apparatus [12]. The acidic environment of the trans-Golgi network triggers a conformational change that allows the host protease furin to cleave prM into the mature M protein [12]. Finally, mature, infectious virions are released from the cell through exocytosis [15].

Pathogenesis and Immunopathology

DENV pathogenesis is distinguished by severe disease often occurring during secondary infection with a different serotype, a phenomenon driven by the host's adaptive immune memory [10,19].

Antibody-Dependent Enhancement

ADE is the central paradigm for severe DENV pathogenesis [20,21]. During a secondary infection, pre-existing, non-neutralizing antibodies from the primary infection bind to the new serotype but fail to neutralize it [17,22]. Instead, Fcγ receptors on myeloid cells recognize these virus-antibody complexes, facilitating more efficient viral entry [18,21].

There are two primary components of ADE:

1. **Extrinsic ADE:** Increases the total number of infected cells by providing an alternative, high-efficiency entry pathway via FcγR [17,21].
2. **Intrinsic ADE:** Modulates the internal cell environment to favor viral production. Binding to FcγRIIA suppresses the production of type I interferons and pro-inflammatory cytokines while increasing the production of anti-inflammatory cytokines like IL-10 [20,21]. This "immune subversion" can lead to a 100-fold increase in viral progeny per cell compared to primary infection [21].

The "Cytokine Storm" and Vascular Leakage

The hallmark of severe dengue is vascular hyperpermeability, leading to plasma leakage into interstitial spaces [18]. This is not caused by direct endothelial cell death, but rather by a cytokine storm and the direct effects of the viral NS1 protein [12,21].

Hyperactivated immune cells, particularly those infected via ADE, release excessive levels of vasoactive mediators and pro-inflammatory cytokines, including TNF- α , IL-6, IL-8, and IL-10 [20,22]. Furthermore, secreted NS1 can directly interact with endothelial cells, leading to the degradation of the glycocalyx—a protective layer on the interior of blood vessels—thereby compromising the endothelial barrier [12,17]. This transient increase in permeability leads to hypotension, circulatory collapse, and potentially fatal shock [11,18].

Clinical Manifestations and Challenges

The clinical spectrum of DENV infection ranges from asymptomatic (up to 75% of cases) to severe systemic disease [7,8]. Classical Dengue Fever presents as an acute febrile illness characterized by severe headache, retro-orbital pain, myalgia, and arthralgia [7,8]. In contrast, DHF and DSS are characterized by thrombocytopenia, hemorrhagic manifestations, and significant plasma leakage [7,17].

The absence of a specific antiviral therapy makes clinical management primarily supportive, focusing on meticulous fluid resuscitation and vital sign monitoring [10,11]. The complexity of the immune response, particularly the risk posed by ADE, remains a significant hurdle in the development of a universally effective tetravalent vaccine [8,10]. Understanding the molecular interplay between viral proteins like NS1 and host restriction factors remains critical for identifying new therapeutic targets to mitigate the global burden of this disease [15,23].

Importance of Seroprevalence Studies

Seroprevalence studies are crucial for understanding the true burden of DENV infection, identifying high-risk populations, and informing public health interventions, particularly given the large proportion of asymptomatic or mild cases that may go unreported [24]. These investigations also provide critical data for evaluating the efficacy of vaccine programs and assessing the long-term impact of various control measures [25]. Specifically, seroprevalence data can delineate the geographical and demographic distribution of immunity, thereby guiding targeted vaccination campaigns and resource allocation for vector control [26]. Furthermore, these studies are instrumental in characterizing the endemicity and epidemic potential of DENV within specific regions, offering insights into the immunological landscape of susceptible populations [12]. Such data are particularly vital in the Caribbean, where several factors, including climate, high population density, and frequent travel, contribute to sustained DENV transmission and the potential for severe outbreaks. The diagnostic challenges associated with dengue, including similarities with other febrile illnesses and the limitations of current rapid diagnostic tools, further underscore the necessity of seroprevalence data to accurately gauge infection rates [27]. This is particularly relevant as cross-reactivity with other flaviviruses can complicate serological diagnostics, further necessitating robust seroprevalence studies to differentiate DENV exposure from other viral infections [28]. Moreover, the identification of dengue serotypes through seroprevalence studies is critical for understanding their individual contributions to disease epidemiology and informing future vaccine development efforts, especially considering the distinct clinical profiles and varying propensities for symptomatic infection observed among different serotypes [29]. This comprehensive understanding of serotype prevalence and distribution is essential for predicting future outbreaks and optimizing public health responses in endemic areas [30]. Such studies are also essential for guiding vaccine introduction policies, as recommended by the Strategic Advisory Group of Experts on Immunization, which advises vaccine deployment only in settings with high endemicity ($\geq 70\%$ seroprevalence) [31].

Overview of Dengue Seroprevalence in the Caribbean

Seroprevalence studies offer invaluable insights into the transmission intensity of dengue, serving as a robust indicator of the cumulative exposure within a population over time [1,32]. In the French Caribbean islands of Guadeloupe and Martinique, a 2011 study on adult blood donors revealed a high seroprevalence of 93.5% for dengue antibodies, with 90.7% in Martinique and 96.2% in Guadeloupe [33]. These findings underscore the pervasive circulation of DENV in these territories and highlight a significant cumulative exposure across the adult population. Conversely, community-based seroprevalence studies, particularly those incorporating age- and gender-standardization, are notably scarce in the broader Caribbean, leaving significant gaps in understanding cumulative exposure, population immunity, and vulnerability to future outbreaks [34]. This data deficit is particularly pronounced for specific dengue serotypes, despite evidence of all four DENV serotypes circulating in the Caribbean region [35]. This deficiency hinders the precise characterization of the epidemiological landscape, thereby complicating the implementation of targeted public health interventions and vaccine deployment strategies. For instance, the recurrent introduction and spread of all four DENV serotypes over the last three decades in the Caribbean underscore the need for continuous surveillance and comprehensive seroprevalence assessments to monitor the changing epidemiological dynamics [36]. Further detailed serological assays, including plaque reduction neutralization tests, are essential to differentiate between monotypic and multitypic immunity and to precisely characterize the specific serotypes that have historically circulated within these diverse island nations [37]. In Jamaica, a seroprevalence study found 100% IgG positivity among healthy individuals, indicating universal past exposure to DENV in the sampled population [38]. However, the absence of detailed age-stratified data and serotype-specific prevalence limits the utility of such broad findings for targeted public health interventions.

Specific Island and Sub-Regional Findings

This gap in comprehensive, serotype-specific data is further exacerbated by the significant population movement throughout the Caribbean, which facilitates the constant introduction and re-introduction of diverse DENV serotypes, posing ongoing challenges for public health surveillance [39,40]. Indeed, genetic sequencing from infected travelers has revealed a widespread diversity of circulating viral lineages across the Caribbean, often with different serotypes driving outbreaks on various islands simultaneously [36]. This dynamic epidemiological landscape underscores the critical need for more robust, island-specific seroprevalence studies that incorporate serotype identification to accurately characterize DENV circulation patterns and inform precise public health strategies [39].

The Caribbean archipelago presents a unique epidemiological landscape for dengue virus transmission, characterized by high levels of endemicity and frequent hyperendemic cycles involving the co-circulation of all four serotypes [2,41]. Comparative global analyses indicate that the Caribbean and the broader Americas exhibit significantly higher seroprevalence rates compared to regions such as Asia or Africa, with variations often exceeding 50 percentage points between different territories [2]. Within this region, seroprevalence is strongly age-dependent, reflecting cumulative exposure over time and a shift in the primary burden of disease toward younger cohorts as adults achieve multitypic immunity [42,43].

Greater Antilles Seroprevalence

The Greater Antilles, comprising the largest islands in the Caribbean, has served as major hubs for DENV research due to their high population densities and complex transmission dynamics [44,45].

JAMAICA

Seroprevalence data from Jamaica reveal a state of near-universal exposure among the adult population. A landmark study utilizing enzyme-linked immunosorbent assay on healthy Jamaican adults identified a 100% (277/277) seroprevalence of dengue IgG antibodies [38]. This ubiquitous

exposure suggests that DENV is hyperendemic, rendering IgG testing of limited diagnostic utility for acute cases in adult populations [38]. Furthermore, 3.6% of the healthy population tested positive for IgM antibodies, with a significantly higher prevalence in males (9.5%) compared to females (0.0%), likely reflecting gender-based differences in occupational or environmental exposure [38]. Studies in pregnant women across Jamaica and St. Kitts and Nevis also corroborated this 100% seroprevalence rate, highlighting the significant risk of vertical transmission or pregnancy complications in these settings [2].

PUERTO RICO

Puerto Rico provides some of the most robust longitudinal data in the region. Modeling of age-specific case data has revealed varying transmission intensities over several decades. In 2010, the estimated seroprevalence for the 18–87-year-old cohort was 95.9%, while the 18–25-year-old group showed a slightly lower rate of 86.9% [46]. Pediatric data from 2007–2008 in the municipality of Patillas found a 42.5% seroprevalence among 10–11-year-olds, which rose to an estimated 57.2% by 2010 [46]. These findings illustrate that a significant proportion of the population is infected multiple times before reaching early adulthood, creating a high-risk environment for antibody-dependent enhancement during subsequent heterologous infections.

CUBA

Cuba's epidemiological history is defined by massive, well-documented outbreaks that have provided critical insights into DENV pathogenesis. During the 1981 DENV-2 epidemic, the inapparent infection rate was estimated at 71% in white individuals and 88% in black individuals, a disparity often attributed to genetic factors or prior immunological priming [47]. This epidemic was particularly severe because approximately 45% of the population had previously seroconverted during the 1977 DENV-1 epidemic, setting the stage for widespread secondary infections [47]. By the 1997 DENV-2 epidemic in Santiago, nearly all secondary infections were clinically overt, whereas only 3–6% of primary infections manifested symptoms [47]. These historical cohorts highlight how seroprevalence is shaped by discrete, large-scale transmission events rather than constant low-level endemicity [48].

HAITI & DOMINICAN REPUBLIC

Data from Haiti suggest early childhood exposure is common. Studies conducted in Port-au-Prince between 1996 and 1999 among children aged 6–14 found high levels of multitypic immunity [48]. More recent surveys in regions such as Gressier and Jacmel continue to show high force-of-infection values, indicating sustained high-intensity transmission [1]. Similarly, in the Dominican Republic, a 2002 study in Santo Domingo among individuals aged 0–60 identified a high prevalence of all four serotypes, characteristic of an urban hyperendemic environment [48].

Lesser Antilles Seroprevalence

The smaller islands of the Lesser Antilles exhibit some of the highest recorded DENV seroprevalence rates globally, often exceeding those found in traditional endemic strongholds in Southeast Asia [41].

FRENCH WEST INDIES

The French Caribbean territories have provided definitive evidence of the extent of DENV penetration in the region. A 2011 prospective study of 783 adult blood donors in Guadeloupe and Martinique found an overall seroprevalence of 93.5% [33]. Specifically, 96.2% of donors in Guadeloupe and 90.7% in Martinique were IgG-positive [33]. Notably, despite this high seroprevalence, only 30% of participants recalled having a symptomatic dengue illness, underscoring

the massive burden of inapparent infections [33]. Neutralization assays on a subset of these samples revealed that 80% of the IgG-positive individuals possessed neutralizing antibodies against all four serotypes, indicating a state of complex, multitypic immunity that may modulate future outbreak patterns [33].

TRINIDAD & TOBAGO

Trinidad remains a high-intensity transmission zone with a reported DENV seroprevalence of 94% [41]. The high transmission intensity in Trinidad is comparable to that of Sint Eustatius, which reported a 90% seroprevalence rate [41].

BARBADOS

The epidemiological profile of Barbados has shifted significantly over the long term. As DENV transmission has become more established, the primary target of infection has moved from naive adults toward adolescents and children [43]. Unlike the male-skewed ratios often reported in Southeast Asia, Barbados exhibits a higher proportion of suspected and confirmed cases among females, a trend mirrored in other American countries [43]. This pattern is likely influenced by the indoor habitat of *Aedes aegypti*, which increases exposure for individuals spending more time in domestic environments [43].

Synthesis of Island-Specific Case Studies

The high seroprevalence observed across the Caribbean islands is driven by several regional factors. Urbanization and the domestic nature of the *Aedes aegypti* vector ensure robust DENV transmission even in smaller island settings [43]. The data from 100% seroprevalence in pregnant women in St. Kitts and Jamaica to the 93.5% rate in French Caribbean blood donors suggest that the entire adult population of the Caribbean is essentially a reservoir of DENV immunity [2,33].

This high level of exposure has profound implications for public health. While widespread immunity may provide some level of protection against large-scale outbreaks of established serotypes, it creates a significant risk for the emergence of severe disease if a new serotype or strain is introduced. The high force of infection in these territories means that children are often exposed to multiple serotypes before the age of 15, requiring pediatric-focused vaccination and surveillance strategies [42,46]. The integration of these island-specific seroprevalence data is critical for refining transmission models and developing effective vector control and immunization programs tailored to the unique Caribbean context [1,2].

Summary of Key Findings

The Caribbean epidemiological landscape is defined by its intense hyperendemicity, with dengue virus transmission dynamics reaching levels of near-saturation in several territories. Evidence from Jamaica demonstrates a remarkable 100% seroprevalence in adults, a finding corroborated by high-intensity transmission data in Puerto Rico (95.9%) and the French West Indies (93.5%) [33,38,46]. This high seroprevalence is a direct consequence of the sustained co-circulation of all four DENV serotypes, facilitated by the widespread presence and domestic adaptation of the *Aedes aegypti* vector [8,43].

At the cellular level, the pathogenesis involves the virus's ability to remodel the host endoplasmic reticulum into specialized replication organelles (vROs), which shield viral RNA from innate immune detection and provide a scaffold for the replication complex [12,16]. The critical mechanism of Antibody-Dependent Enhancement remains the primary driver of disease severity during secondary infections. Non-neutralizing antibodies from prior exposure facilitate viral entry through Fcγ receptors on myeloid cells, leading to immune subversion and a 100-fold increase in viral progeny compared to primary infections [20,21]. This process triggers a massive "cytokine storm" involving vasoactive mediators like TNF-α and IL-6 [20,22]. Concurrently, the direct action of

the secreted NS1 protein on the endothelial glycocalyx results in the hallmark vascular hyperpermeability and plasma leakage that define severe dengue [17,18].

Overall Significance for Dengue Control

The transition of DENV from sporadic outbreaks to established hyperendemicity in the Caribbean necessitates a fundamental shift in control and diagnostic strategies. Because IgG antibodies are essentially ubiquitous in adult populations across islands like Jamaica and St. Kitts, standard serological IgG testing is largely ineffective for acute diagnostic purposes; protocols must instead prioritize NS1 antigen detection or RT-PCR to distinguish current infections from past exposure [10,38]. Furthermore, the observation that a vast majority of infections remain inapparent implies that clinical surveillance alone significantly underestimates the true transmission potential within these communities [7,33].

This "silent" transmission reservoir renders traditional, reactive mosquito control efforts—such as fogging after cases are reported—largely ineffective. Integrated vector management must therefore emphasize year-round, proactive source reduction and community-based environmental management [13,43]. Regarding immunization, the high regional seroprevalence presents a complex challenge; while vaccination is critical for protecting increasingly vulnerable pediatric populations, the risk of ADE mandates the use of balanced tetravalent vaccines to ensure that immunization does not inadvertently prime individuals for severe secondary-like responses [8,10]. Finally, the longitudinal shift of the disease burden toward younger cohorts, as documented in Barbados, highlights the urgent need for targeted school-based screening and specialized pediatric clinical training to manage the specific risks of severe dengue in children [42,43]. Enhanced regional collaboration and sustained genomic surveillance are essential to track viral evolution and mitigate the threat of novel, potentially more virulent DENV strains entering the highly primed Caribbean population [4,41].

Future Perspectives

Future research endeavors should prioritize the development and implementation of advanced genomic surveillance techniques, enabling real-time monitoring of DENV serotype prevalence and the emergence of novel genotypes, efforts should be focused on understanding the immunological correlates of protection and risk in individuals with pre-existing immunity to better inform vaccine development and deployment strategies for hyperendemic regions [49]. Furthermore, given the documented high seroprevalence rates, investigation into the potential for antibody-dependent enhancement in the context of vaccine implementation is crucial [50]. Efforts to improve passive surveillance systems by incorporating active surveillance methods and enhancing the detection of inapparent infections are imperative to rectify the underreporting of febrile dengue infections [51]. This includes the development of cost-effective diagnostic tools for rapid, accurate detection in resource-limited settings and continuous training for clinical staff on early identification and appropriate intervention [52]. Moreover, a deeper understanding of serotype-specific patterns of inapparent DENV infections across diverse geographic regions is essential, as the complex serotype dynamics observed in one setting may not be generalizable to others with varying flaviviral landscapes [29]. This underscores the necessity for region-specific studies to characterize seroprevalence and transmission dynamics accurately, especially in areas with co-circulating flaviviruses which may influence diagnostic accuracy and immune responses [53].

Conclusion

The hyperendemic status of the Caribbean, characterized by the near-universal seroconversion of adult populations, emphasizes a profound public health challenge. Longitudinal data from Jamaica and the French West Indies, demonstrating seroprevalence rates of 100% and 93.5% respectively, indicate that DENV exposure is an inevitable epidemiological milestone for the region's

inhabitants [33,38]. This saturated immunological landscape provides a fertile ground for Antibody-Dependent Enhancement, where non-neutralizing antibodies from primary infections facilitate viral entry via Fcγ receptors, leading to immune subversion and a 100-fold increase in viral progeny [17,21].

The molecular pathogenesis of severe dengue is further exacerbated by the "cytokine storm" and the direct action of the NS1 protein on the endothelial glycocalyx, resulting in the hallmark vascular hyperpermeability observed in DHF and DSS [12,18,20] as the disease burden shifts toward younger, immunologically naive cohorts -a trend documented in Barbados and Puerto Rico -the urgency for specialized pediatric surveillance and clinical management becomes paramount [43,46], ultimately, the ubiquitous nature of DENV IgG antibodies in the Caribbean renders traditional serological testing inadequate for acute diagnosis, necessitating a transition toward molecular tools like RT-PCR and NS1-based assays [10,38].

Sustainable control will require a paradigm shift that integrates high-resolution genomic surveillance with the implementation of balanced tetravalent vaccines specifically designed to navigate the region's complex immunological priming [4,8]. Addressing these challenges is essential to breaking the cycle of recurrent outbreaks and mitigating the systemic impact of dengue virus in this highly vulnerable archipelago [20].

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