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Human Genetics and Dengue Vaccination: Ethical, Social, and Humanistic Perspectives on Emerging Challenges and Future Directions

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Abstract

Dengue virus (DENV) infection presents a critical public health crisis across tropical and subtropical regions, including Bangladesh. While clinical manifestations range from mild self-limiting febrile illness to severe dengue shock syndrome, recent bio-medical frameworks highlight the interplay between host genetic variability and vaccine efficacy. Beyond immunological mechanisms, the introduction of dengue vaccines and genetic profiling introduces complex bioethical, social, and humanistic dilemmas regarding equitable access, informed consent, and health equity. This study explores the intersection of host genetic polymorphisms and dengue vaccination strategies, critically examining the ethical, social, and humanistic challenges arising from genomic risk stratification and vaccine deployment in low- and middle-income countries (LMICs). A comprehensive analytical and bioethical narrative synthesis was conducted, re-evaluating molecular epidemiological data alongside socio-ethical frameworks. Genetic variants governing immune regulation (e.g., TNF, IL6, IL10, TLR3, TLR4, FCGR2A, CD209, and MBL2) were analyzed in conjunction with vaccination dynamics, vaccine-induced antibody-dependent enhancement (ADE), and global bioethics guidelines. Genomic risk stratification promises personalized public health interventions but risks exacerbating health disparities, genetic discrimination, and social stigma. Integrating humanistic perspectives into dengue immunization policies is vital for safeguarding vulnerable populations, maintaining institutional trust,

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and ensuring bioethical integrity in national health frameworks.

Keywords: Dengue Vaccination, Host Genetics, Bioethics, Humanistic Perspectives, Health Equity, Genetic Polymorphism, Public Health Policy.

1. Introduction

Dengue fever, caused by four antigenically distinct serotypes of the dengue virus (DENV-1 to DENV-4), remains an expanding vector-borne threat across tropical and subtropical belts (World Health Organization [WHO], 2026). In endemic regions such as Bangladesh, annual outbreaks place immense strain on healthcare infrastructure, causing severe morbidity, plasma leakage, and mortality (Rahim et al., 2023; WHO, 2012). Despite advancements in diagnostic protocols, predicting individual disease severity and vaccine responsiveness remains challenging due to the intricate interplay between viral genetics, host immune status, and underlying genetic polymorphisms (Candrasari et al., 2026; Xavier-Carvalho et al., 2017).

The development and implementation of dengue vaccines (such as Dengvaxia and QDENDA) marked a landmark milestone in tropical medicine. However, dengue vaccination is uniquely complicated by host genetic factors and antibody-dependent enhancement (ADE), wherein pre-existing or vaccine-induced sub-neutralizing antibodies facilitate severe viral replication in secondary exposures (Centers for Disease Control and Prevention [CDC], 2026; WHO, 2026). Furthermore, as precision medicine advances, pre-vaccination genetic screening and host susceptibility profiling have emerged as potential public health tools. This technological evolution brings significant bioethical, socio-economic, and humanistic challenges. Issues concerning genetic privacy, informed consent in vulnerable populations, equitable distribution of biological interventions, and institutional distrust demand rigorous scholarly interrogation.

2. Methodological & Theoretical Framework

To analyze the multi-layered intersection of genomic science, clinical management, and humanistic values, this study synthesizes molecular data with socio-ethical principles. The framework investigates three interdependent domains:

1. **Genomic & Immunological Vectors:** Examination of host genetic variants in immune regulation genes (including *TNF*, *IL6*, *IL10*, *TLR3*, *TLR4*, *FCGR2A*, *CD209*, and *MBL2*) and their influence on vaccine immunogenicity and severe dengue manifestation (Figueiredo et al., 2016; Stephens, 2010; Vieira et al., 2025).
2. **Bioethical Evaluation:** Application of classic bioethical principles—autonomy, non-maleficence, beneficence, and distributive justice—to pre-vaccination screening and vaccine rollouts in resource-limited settings.

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3. **Humanistic & Socio-Cultural Dynamics:** Assessment of institutional trust, stigmatization of genetically susceptible cohorts, and community engagement in global health policy.

3. Host Genetics and Dengue Immunology: The Biological Baseline

Understanding the ethical imperatives of dengue vaccination requires a foundational review of host-pathogen interactions. Host genetic polymorphisms significantly govern how individuals process DENV infection and respond to live-attenuated or subunit vaccines. Key genetic markers implicated in variable clinical outcomes are summarized below:

Gene / Polymorphism	Biological Function	Clinical & Immunological Impact
FCGR2A	Encodes Low Affinity IIa Receptor for IgG Fc Fragment	Modulates antibody-dependent enhancement (ADE); influences uptake of virus-antibody complexes during secondary infection or post-vaccination.
IL10 & IL6	Anti-inflammatory & Pro-inflammatory Cytokine Encoding	Promotes altered cytokine cascades, leading to severe vascular permeability, plasma leakage, and dengue shock syndrome (Vieira et al., 2025).
TLR3 & TLR4	Toll-like Receptors involved in Innate Immunity	Alters double-stranded RNA recognition, modulating early antiviral interferon responses (Candrasari et al., 2026).
MBL2	Mannose-Binding Lectin 2 (Complement System)	Low-producing MBL2 genotypes correlate with impaired opsonization and increased susceptibility to severe dengue bleeding (Figueiredo et al., 2016).
CD209 (DC-	Dendritic Cell-Specific	Acts as a primary cellular receptor for

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Gene / Polymorphism	Biological Function	Clinical & Immunological Impact
SIGN)	Intercellular Adhesion Molecule	DENV attachment; variations dictate initial viral entry dynamics.

While these genetic loci offer targets for risk stratification, applying them within public health programs necessitates resolving key ethical and logistical questions (Xavier-Carvalho et al., 2017).

4. Ethical Dimensions of Dengue Vaccination and Genetic Screening

4.1. Informed Consent and Risk Communication in Vulnerable Populations

A primary bioethical challenge in dengue vaccination strategies involves transparent communication regarding risk, particularly concerning serostatus and genetic susceptibility. Deploying dengue vaccines in populations with high rates of seronegativity or specific genetic predispositions introduces non-trivial risks of severe disease upon subsequent viral exposure (CDC, 2026; WHO, 2026). Obtaining valid informed consent requires explaining complex immunological concepts—such as serostatus screening, genetic susceptibility, and ADE—to individuals across diverse literacy backgrounds without provoking undue panic or vaccine hesitancy.

4.2. Genomic Privacy, Discrimination, and Stigmatization

Integrating host genetic testing into public health vaccination frameworks raises concerns over genomic privacy. If genetic markers (e.g., high-risk *FCGR2A* or *IL10* variants) are identified, individuals could face social stigmatization, being labeled as "hyper-susceptible" or "disease vectors." Without robust legislative protections, genetic information could be misused by commercial entities, employers, or health insurers, violating personal privacy rights and exacerbating socio-economic vulnerabilities.

4.3. Distributive Justice and Health Equity

The principle of distributive justice demands that the benefits and burdens of biomedical research be distributed fairly across society. In developing nations like Bangladesh, introducing expensive pre-vaccination screening technologies or specialized genetic assays risks creating a tiered healthcare system. Wealthier urban segments might access personalized risk profiling and safe vaccination, while marginalized rural populations remain exposed to broad, unmonitored rollouts or lack access entirely. Public health policy must prioritize

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equitable resource distribution to prevent widening existing health disparities (WHO, 2012, 2026).

5. Social and Humanistic Perspectives

5.1. Restoring and Maintaining Institutional Trust

Public health interventions depend directly on societal trust in governance and medical institutions. Historical missteps in vaccine rollouts internationally demonstrate how inadequate risk communication can erode community confidence. Humanistic approaches emphasize transparent policy-making, active community engagement, and clear accountability mechanisms to ensure that vaccination programs foster long-term institutional trust.

5.2. Navigating Cultural Perceptions and Health Literacy

Health decisions are mediated by cultural beliefs, social structures, and lived experiences. In low-resource settings, imposing top-down bio-genomic frameworks without accounting for local cultural perspectives can lead to community resistance. Humanistic health strategies advocate for co-designing public health campaigns with local leaders, civil society organizations, and community healthcare workers to align scientific advancements with local values and ethical priorities.

6. Emerging Challenges & Future Directions

To align advancements in human genetics and dengue vaccination with ethical and humanistic standards, international stakeholders and national health authorities should consider the following strategic priorities:

- **Integrated Ethical Governance:** Establish multi-disciplinary bioethics committees comprising geneticists, bioethicists, public health officials, and community representatives to oversee vaccine trials and genomic data collection.
- **Equitable Infrastructure Development:** Invest in accessible, low-cost diagnostic infrastructure to ensure pre-vaccination screening and risk assessment are universally available, eliminating financial barriers for vulnerable demographics.
- **Robust Legislative Protections:** Enact stringent national data protection regulations guarding personal genomic data against unauthorized commercial access or discriminatory use.
- **Humanistic Health Communication:** Develop culturally nuanced risk communication strategies that demystify genetic screening and vaccine dynamics, empowering individuals to make informed decisions.

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- **Multicenter Population Research:** Encourage population-specific genomic research tailored to South Asian cohorts, avoiding the inappropriate application of Western-centric genetic models to local healthcare settings (Rahim et al., 2023).

7. Conclusion

The convergence of human genetics and dengue vaccination represents a promising frontier in tropical medicine, offering tools to mitigate severe clinical outcomes. However, technical innovation alone cannot resolve systemic health challenges. Incorporating bioethical rigor, social justice, and humanistic values into public health policy is essential. By addressing issues of informed consent, genetic privacy, health equity, and institutional trust, global health systems can ensure that genomic advancements serve as instruments of social good rather than sources of inequality.

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