

Review

A Review of Pathogens Transmitted by the Container-Inhabiting Mosquitoes, *Aedes Albopictus*, A Global Public Health Threat

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ABSTRACT

Dengue virus (DENV), Chikungunya virus (CHIKV), and Zika virus (ZIKV) are highly pathogenic human arboviruses transmitted by the *Aedes (Stegomyia) albopictus* (Skuse) (Diptera: Culicidae) or *Ae. Albopictus* mosquito. These arboviruses are responsible for causing fever, hemorrhagic conditions, and neurological diseases in humans post-bite from an infected *Aedes* mosquito. Over the past 80 years, the *Ae. albopictus* has infested every habitable continent, bar Antarctica, thereby escalating the probability of global insect-borne infectious disease outbreaks. This research follows the global transmission pattern of *Ae. albopictus* and provides a summary of disease prevention and control strategies for mosquito-borne infections, as implemented by the World Health Organization (WHO) and both Asian and European countries. Consequently, this study can aid in the prevention and control of mosquito-borne diseases while acting as a basis for international collaboration on effectively managing arbovirus infection issues in public health.

INTRODUCTION

Globally, 537 arboviruses have been identified, with over 150 presenting a significant risk for transmission to humans or animals (1). *Ae. albopictus* serves as a vector for several highly pathogenic viruses to humans, including Dengue, Chikungunya, Zika virus, among others. Over the last three to four decades, the presence of *Ae. albopictus* has been reported in more than 70 countries, extending its global distribution to all continents except Antarctica (2). A recent study developed a model predicting the presence of *Ae. albopictus* in 197 countries by the year 2080 (3).

Global socioeconomic development, rapid urbanization, increased human and goods mobility, and climate change have all contributed to an escalating risk of vector-borne diseases. Moreover, with

the resurgence of regional and international population movement and trade transactions as the world begins to navigate the post era of Coronavirus 2019 (COVID-19) pandemic, the global spread of vector-borne viruses has similarly increased. This study seeks to provide an overview of pathogenic virus species and infection rates carried by *Ae. albopictus* worldwide, summarizing strategies undertaken by global organizations for mosquito-borne disease prevention and control across various regions in furtherance of One Health objectives.

AEDES ALBOPICTUS

The *Aedes (Stegomyia) albopictus* (Skuse) (Diptera: Culicidae), more commonly known as the Asian tiger mosquito, originates from Southeast Asia but is broadly dispersed within tropical and subtropical regions, particularly thriving and reproducing in densely populated urban environments. It exhibits peak activity during daylight hours (4). Its vectoring competency is lower than that of *Aedes aegypti* (*Ae. aegypti*), notwithstanding, its higher tolerance to colder climates allows for a wider range of dispersion (5). Upon biting and feeding on animal or human hosts, *Ae. albopictus* transmits pathogenic viruses, thereby causing symptoms of disease.

PATHOGENIC PATHOGENS

Current research indicates that *Ae. albopictus* mosquitoes can transmit numerous pathogens including Dengue virus (DENV), Zika virus (ZIKV), Chikungunya virus (CHIKV), Japanese encephalitis virus (JEV), West Nile virus (WNV), Mayaro virus (MAYV), and Tahyna virus (TAHV), among others, prompting outbreaks and epidemics of vector-borne diseases in assorted regions (4). In the ensuing section, we will provide a detailed analysis of the pathogenic viruses that *Ae. albopictus* can harbor.

Dengue virus: The DENV belongs to the *Flavivirus*

genus within the family Flaviviridae, encompassing four primary serotypes: DENV-1, DENV-2, DENV-3, and DENV-4. These serotypes are globally prevalent. However, the Mustafa study discovered a potential fifth serotype (1). Dengue fever (DF) manifestations differ across serotypes, typically initiating with a rapid onset of high fever, headache, back, bone, joint, and muscle pain, petechiae on the skin, swollen lymph nodes, and a reduction of white blood cells and platelets. DENV was initially isolated in Japan in 1943 from the serum of an infected patient using suckling mice (6). The first recorded outbreaks of DF occurred in Jakarta, Indonesia, and Cairo, Egypt, in 1779 (7). Currently, DF is acknowledged as the most widespread and rapidly proliferating mosquito-borne viral disease affecting humans, with high prevalence in Africa, Asia, Australia, and the Americas (8). *Ae. aegypti* and *Ae. albopictus* are key vectors in DENV transmission (5). Interestingly, the virus was first isolated from *Ae. albopictus* females captured during an outbreak in Libreville, Gabon, while all *Ae. aegypti* specimens tested negative (9). Genotype 1 DENV was detected in *Ae. albopictus* mosquitoes sampled during a localized DF outbreak in Wenzhou City, Zhejiang Province, China, in 2018 (10). Moreover, positive DENV isolation rates from *Ae. aegypti* and *Ae. albopictus* in China were found to be 13% and 1%, respectively (10). Another study reported an 8.33% DENV-positive rate in *Ae. albopictus* overwintering eggs collected from the West Lake area in Hangzhou (11).

Zika virus: The ZIKV is a *Flavivirus* arbovirus characterized by two distinct subtypes: African and Asian. ZIKV infection symptoms can include low-grade fever, maculopapular rash, headaches, arthralgia, myalgia, weakness, and nonsuppurative conjunctivitis. The virus was first identified in 1947 from a rhesus monkey inhabiting the "Zika jungle" in Kampala, Uganda and later found in *Ae. aegypti* mosquitoes within this same forest (12). The inaugural human case of ZIKV was reported in Nigeria in 1954 (13).

Starting from May 2015, the virus has sparked large-scale outbreaks across the Americas, most notably, in Brazil. Of considerable concern is the association of ZIKV infections in pregnant women with fetal microcephaly. This link has catapulted the Zika disease into a global health concern and contributed to ZIKV's spread to 59 countries across the globe (14).

While *Ae. aegypti* has been identified as the primary mosquito vector transmitting ZIKV, the virus has also been confirmed in *Ae. albopictus* and *Aedes africanus* mosquitoes (15). Research by Jeronimo Alencar and

colleagues has unveiled ZIKV infections and natural vertical transmission within Brazil's *Ae. albopictus* (16). In 2020, a study in China investigated the oral susceptibility and vector competence of ZIKV within *Ae. albopictus* Guangzhou beads. It was discovered that, six days after infection, a prevalence of 36.4% of the virus was found in the saliva of *Ae. albopictus* mosquitoes (17).

Chikungunya virus: CHIKV falls under the *Togaviridae* family, specifically the genus *Alphavirus*. It boasts four genotypes: West African (WA), East/Central/Southern African (ECSA), Asian, and Indian Ocean type (IOL) (18). Typical manifestations of the virus's acute phase are sharp instances of fever, arthralgia affecting the knees and shoulders, and extreme pain due to arthritis. Initially identified in 1953, CHIKV originates from Africa, with the first isolation recorded in Tanzania. The inaugural *Ae. albopictus*-vectored strain of CHIKV, appearing as an IOL strain, was discovered on Reunion Island in the Indian Ocean (19). In Italy, CHIKV's genome has been identified within the *Ae. albopictus* mosquito, pointed as the vector instigating local Chikungunya fever outbreaks (4). Current epidemiological studies have not produced evidence suggesting that *Ae. albopictus* can transmit the Asian genotype of CHIKV (18). The mosquito-borne illness, once restricted to South Africa, Southeast Asia, and selective tropical regions in India, has now breached other subtropical nations (18). Evolution of CHIKV enhances its compatibility with *Ae. aegypti* or *Ae. albopictus*, thereby improving the virus's transmission within populations. CHIKV's main adaptation for increased infectivity is promoting the reproductive capabilities of *Ae. Albopictus* (18).

Japanese encephalitis virus (JEV): JEV is a zoonotic disease transmitted by mosquitoes. While infection is often asymptomatic, severe cases can lead to acute encephalitis and neurological sequelae (20). Classified under the *Flavivirus* genus of the *Flaviviridae* family, JEV is a single-stranded positive-stranded RNA virus. Five genotypes of JEV exist, with genotype 1 strains increasingly prominent in China (21). Currently, JEV is endemic in 24 countries across South and Southeast Asia, Japan, northern Australia, and Oceania (22). Seventeen species of mosquitoes are known to transmit JEV, while an additional ten species are potential carriers (20). *Aedes darkis*, *Aedes mansoni*, *Aedes* spp., and *Culex trituberculatus* (*Cx. trituberculatus*) serve as vectors for JEV, with *Cx. trituberculatus* acknowledged as the primary vector in China and most other Asian

countries (22). JEV was first discovered in Taiwan, China, in 1895, with its isolation from *Ae. albopictus* yielding a minimum infection ratio (MIR) of 0.56% (23). Subsequent research has demonstrated that JEV can survive for two months in desiccated *Ae. albopictus* eggs (24).

West Nile virus (WNV): a member of the *Flaviviridae* family, is a zoonotic arbovirus transmitted between mosquitoes and birds. Humans and other animals primarily act as terminal hosts. WNV has been responsible for diseases in humans across all continents except Antarctica (25). Most individuals infected with WNV remain asymptomatic, while a minute fraction manifests symptoms such as WNV encephalitis, meningoencephalitis, and meningitis (26). The virus has been reported in Africa, Asia, Europe, Australia, and North America, identifying it as the most widely spread mosquito-borne *flavivirus* globally (27). The risk of acquiring a vector-borne disease through a mosquito bite remains substantial, and the virus has been detected in a variety of mosquito species, including *Aedes* (28), *Anopheles* (29), and *Culex* mosquitoes (30). WNV was first isolated in Chinese mainland in 2011 from mosquitoes in Jiashi County, Kashgar Region, Xinjiang, following outbreaks of viral meningitis and encephalitis caused by WNV (31). In laboratory experiments, Chinese researchers fed *Cx. trituberculatus*, *Cx. quinquefasciatus*, *Cx. pipiens*, and *Cx. bitaeniorhynchus* mosquitoes blood infected with WNV. They found that all four mosquito species could transmit the virus, with *Cx. trituberculatus* showing the highest infection and transmission rates (87.5% and 74.2%), respectively (30). Some studies have identified local WNV transmission in China through serological assays (27). Moreover, experimental studies have demonstrated that WNV can survive in *Ae. albopictus* eggs and continue to be transmitted to mosquito larvae once the latency is disrupted (28).

Mayaro virus: The Mayaro virus (MAYV; family *Togaviridae*, genus *Alphavirus*) is a single-stranded positive-stranded RNA virus, which produces symptoms akin to DENV infection, with acute joint pain being the most prominent clinical symptom of MAYV infection (32). The virus was first isolated in 1954 from ailing forestry workers in Trinidad, while subsequent instances of human infection and minor outbreaks have been documented in northern regions of South America (33–34). Although the majority of recorded cases have been associated with humid, flood-prone forested areas, there has been an increasing,

worrisome trend towards urbanized cases of MAYV transmission (35–36). Presently, the virus is primarily endemic in South America, with Brazil being the most affected (37). Various mosquito species, including *Ae. aegypti*, *Culex*, and *Ae. darkis* are vectors of MAYV transmission (33). Research conducted on the Brazilian strain of *Ae. albopictus* indicates that this species can act as a vector for MAYV transmission, contingent upon a sufficiently high population and extensive incubation period to allow virus proliferation (38).

Tahyna virus (TAHV): TAHV originated from the *Bunyaviridae* family, specifically, the genus *Orthobunyavirus* within the California serogroup. Infections typically manifest in the form of fever and flu-like symptoms. However, it can also lead to more severe conditions such as pneumonia and pleurisy, acute arthritis, pharyngitis, and in rare instances, central nervous system dysfunction. TAHV holds the distinction of being the first arbovirus isolated in Europe, specifically from *Aedes. Caspius* and *Aedes. Vexans* collected in the Tahyna and Krizany villages in Eastern Slovakia (39). The virus subsequently spread throughout Europe, with Calzolari et al. (2021) discovering a 4% positivity rate in *Ae. albopictus* during mosquito surveillance in Emilia-Romagna (40). TAHV was first isolated in China from *Culex* mosquitoes in Xinjiang in 2006, with subsequent potential human transmission inferred from seropositive tests among febrile patients (41). Since then, the virus has also been identified in other mosquito species in Qinghai and Inner Mongolia (42).

CARRIAGE STATUSES OF COMPOUND VIRUSES

Ae. albopictus mosquitoes function as carriers of DENV, CHIKV, and MAYV, among other viruses. As a result, regions inhabited by this mosquito species often experience a high incidence of viral co-vectors and multiple instances of mosquito-borne illnesses within their populations. In an increasing volume of investigations, this particular vector has been found residing simultaneously alongside multiple viruses. Wazeye 2010 first identified the potential for a single *Ae. albopictus* mosquito to contract both CHIKV and DENV during a controlled infection experiment (43). The first reported case of Dengue-Chikungunya co-infection took place in Thailand in 1962 as documented by Nimmannitya et al. (44). Instances of worldwide Dengue-Chikungunya co-infections have been found and continue to exist in such regions as

Africa, Southeast Asia, the Eastern Mediterranean, and the Western Pacific (43). There are even reports of three patients having Dengue, Chikungunya, and Zika co-infections presenting with fever syndrome along the Colombia-Venezuela border (45). Genetic testing conducted on an 8-year-old boy from Haiti in 2015, residing in a non-forested region and exhibiting fever symptoms, demonstrated infections of both DENV-1 and MAYV (46).

Prevention and Control Policies for Vector-Borne Diseases

The global community is showing growing concern over mosquito-borne diseases. Consequently, the proactive prevention and control of arthropod diseases has become a widely discussed topic of paramount importance.

The global propensity for zoonotic diseases to cross borders necessitated a comprehensive approach, which led the American Veterinary Medical Association (AVMA) to introduce the “One Health” concept in 2007. This term encapsulates the intricate interplay between humans, animals, and the environment in the propagation of diseases. Critical issues addressed by One Health encompass zoonotic afflictions, antimicrobial resistance, food safety and security, vector-borne diseases, environmental contamination, and various other health challenges common to humans, animals, and the environment. The promotion of the One Health ethos is fostering opportunities for establishing frequent interrelationships between public health disciplines and ancillary fields, thus facilitating interdisciplinary cooperation in education and scientific research.

In October 2015, the Fifth Plenary Session of the 18th Central Committee of China’s Communist Party (CPC) officially stated the upcoming 15-year span as a crucial strategic opportunity for enhancing the establishment of a healthier China. This undertaking represents a significant initiative to proactively contribute towards global health governance and meet the international obligations of the 2030 Agenda for Sustainable Development.

In October 2016, China’s Communist Party Central Committee and the State Council issued the blueprint for the “Healthy China 2030” initiative. This program showcases an expansive plan of action focused on advancing the protection of citizen health. It articulates the infrastructural provisions necessary for safeguarding the public’s health. The outline details China’s pledge

to conduct wholesome patriotic health movements, implement a thorough control and prevention strategy against disease-bearing organisms primarily through environmental management, and to manage the health concerns in both urban and rural environments synergistically.

Moreover, by 2030, China aspires to establish numerous exemplar cities, towns, and villages to support the notion of healthy living. Plans also include setting up state-of-the-art monitoring and early warning systems for global infectious disease information, enhancing the international travel health information network, offering real-time and efficient health guidelines for global travel, and constructing a world-class international travel health service system to safeguard the wellbeing and safety of international arrivals and departures.

Finally, China intends to enhance the surveillance and control mechanisms aimed at disease carriers and various major infectious diseases at international border crossings. Proactive efforts will be directed toward preventing, controlling, and responding to public health emergencies originating outside the country.

In light of the global duality of threat and burden posed by both new and re-emerging vector-borne diseases and imported and endemic vector-borne diseases, the 70th World Health Assembly initiated the “Global Vector Control Response 2017–2030” in 2017. This action plan indicates that 80% of the global population is at risk from one or more vector-borne diseases, 17% of the global burden of infectious diseases is attributable to vector-borne infections, and each year, vector-borne diseases cause more than 700,000 fatalities (47). Countries across the globe have begun to implement innovative prevention and control strategies, heralding a new era for the international prevention and control of vector-borne diseases.

As outlined in the 2020 WHO Vision for the Future of Work with Western Pacific Member States and Partners Towards the Healthiest, Safest Regional Future, the gravest collective concern for the Western Pacific region revolves around the health impacts of climate and environmental changes. The WHO remains steadfast in its commitment to addressing the “unfinished business” of controlling and eliminating infectious diseases as public health threats (48).

In 2022, China put forth plans to finalize its public health infrastructure, bolster its main epidemic prevention and treatment protocol, and enhance its emergency response capabilities. This move aimed to

effectively manage the propagation of critical infectious diseases. Concurrently, a national administration for disease prevention and control was established, assuming full responsibility for mitigating disease and especially curtailing the sudden outbreak of infectious diseases. Alongside these structural revisions, the government vowed to foster outstanding talent capable of addressing substantive public health challenges. Additionally, there is an emphasis on significantly augmenting the caliber of scientific research in disease prevention and control sectors, with a particular focus on nurturing expertise in tracing infectious disease origins.

TECHNIQUES AND STRATEGIES FOR VECTOR CONTROL

At present, most virus-specific drugs and vaccines for mosquito-borne diseases are in the developmental stages, with their safety and efficacy yet to be definitively established. Consequently, preventative measures and control strategies for these diseases emphasize the primordial tenets of “controlling the source of infection, obstructing the transmission route, and protecting the vulnerable population”. The Centers for Disease Control and Prevention (CDC) advocates for mosquito vector management and bite avoidance as the primary preventative measures for mosquito-borne diseases such as Dengue, Zika, and Chikungunya. Essential to these efforts are robust systems for monitoring mosquito vectors, rapidly detecting and curbing potential epidemics (49).

Some researchers propose that, in countries where *Ae. albopictus* has not yet established a foothold, the primary focus should be on refining the detection of this species at entry points and beyond, leveraging advancements in vector biomonitoring and genomic technologies (3). A comprehensive practical study on effective mosquito vector control methods in Latin America and the Caribbean suggests that an integrated approach that emphasizes community engagement appears most effective in reducing the transmission of diseases through *Ae. mosquitoes* (50).

China’s commitment to public health is reflected in their explorations of the “One Health” concept and innovative initiatives such as the “Mosquito-Free Village” pilot project launched in Zhejiang Province in 2016. The project, a grassroots effort targeted at long-term vector control, set the stage for the province’s development in 2021 of the first phase of the

“mosquito and fly eradication villages.” This initiative provides both a theoretical and practical foundation for environmentally sustainable, long-lasting programs focused on biological vector management and the prevention and control of mosquito-borne disease outbreaks, such as dengue fever (51).

These programs emphasize the use of environmental, physical, and chemical control measures to decrease the population and reproductive capacity of mosquito vectors, thereby reducing the risk of mosquito-borne virus transmission to humans. Concurrently, each district implements active mosquito monitoring programs tailored to the locale’s geographical and climatic attributes. Additionally, local communities are encouraged to participate in integrated disease vector organism management efforts (52).

CONCLUSION

The mosquito-borne virus carried by *Ae. albopictus* is now highly prevalent and globally transmitted, significantly affecting not only human health but also the worldwide economic landscape. A comprehensive examination of these mosquito-borne viruses, with a focus on the molecular analysis of their genomes, will help in the development of vaccines and effective therapeutic options. Consistent monitoring of mosquito populations that serve as carriers, combined with risk assessment and forecasting through mathematical models, aids in the early identification of potential disease outbreaks and epidemics. Every nation bears a responsibility to aid in thwarting the dissemination of arboviruses. Further, the practice of sharing consolidated and successful prevention and control strategies will bolster efforts to achieve the One Health objective.

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