Journal of Mosquito Research, 2024, Vol.14, No.5, 247-255
http://emtoscipublisher.com/index.php/jmr

Research Insight Open Access

Environmental and Ecological Factors Influencing Japanese Encephalitis Transmission

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Journal of Mosquito Research, 2024, Vol.14, No.5 doi: 10.5376/jmr.2024.14.0023
Received: 07 Sep., 2024
Accepted: 10 Oct., 2024
Published: 21 Oct., 2024

Preferred citation for this article:
Luo Q.Y., and Xu X.Y., 2024, Environmental and ecological factors influencing japanese encephalitis transmission, Journal of Mosquito Research, 14(5): 247-255 (doi: 10.5376/jmr.2024.14.0023)

Abstract Japanese Encephalitis (JE) is a significant vector-borne zoonotic disease primarily affecting Southeast Asia, with potential for expansion into new regions due to various environmental and ecological factors. This study examines the multifaceted influences on JE transmission, including vector ecology, climate variables, and anthropogenic changes. The primary vectors, predominantly *Culex* species, play a crucial role in the transmission dynamics, with environmental conditions such as temperature, rainfall, and humidity significantly impacting vector competence and virus dissemination. Additionally, the role of amplifying hosts like pigs and birds, along with the potential for new vector species to emerge in non-endemic regions, underscores the complexity of JE epidemiology. Increased surveillance, vector control, and public health interventions are essential to mitigate the risk of JE outbreaks in both endemic and susceptible regions. This study synthesizes current knowledge and identifies gaps for future research to better understand and control JE transmission.
Keywords Japanese encephalitis; Vector ecology; Climate change; Zoonotic disease; *Culex* mosquitoes

1 Introduction

Japanese Encephalitis (JE) is a viral disease primarily found in Southeast Asia and the Western Pacific regions. It is caused by the Japanese Encephalitis Virus (JEV), which is transmitted to humans through the bite of infected mosquitoes, predominantly of the *Culex* species (Pearce et al., 2018; Srivastava et al., 2023). The disease is zoonotic, with pigs and birds serving as the main amplifying hosts, while humans are considered dead-end hosts (Ladreyt et al., 2019). JE is a significant public health concern due to its high morbidity and mortality rates, with an estimated 67,000 cases reported annually. Despite the availability of vaccines, JE remains the leading cause of viral encephalitis in many Asian countries.

Understanding the environmental and ecological factors influencing JE transmission is crucial for several reasons. Firstly, the distribution and abundance of mosquito vectors are heavily influenced by climatic conditions such as temperature, rainfall, and humidity, which in turn affect the transmission dynamics of JEV. For instance, studies have shown that increases in temperature and humidity can enhance mosquito development and virus transmission rates (Singh et al., 2020). Secondly, changes in land use, urbanization, and agricultural practices can alter the habitats of mosquito vectors and amplifying hosts, thereby impacting JE epidemiology (Pearce et al., 2018). Additionally, the emergence of new JEV genotypes in novel ecological settings, such as the recent outbreaks in Australia, underscores the need for continuous surveillance and understanding of these factors to predict and mitigate future outbreaks (Hurk et al., 2022; Mackenzie et al., 2022).

This study synthesizes current knowledge on the environmental and ecological factors that influence the transmission of Japanese Encephalitis (JE), focusing on identifying and evaluating key environmental variables that affect the distribution and abundance of JE vectors, assessing the role of ecological factors such as land use changes and host-vector interactions in transmission dynamics, examining the impact of climate change on the potential expansion of JE into new geographic areas, and providing recommendations for improving surveillance and control strategies based on these factors, with the aim of contributing to a better understanding of JE transmission and informing public health interventions to reduce the burden of this disease.

2 Overview of Japanese Encephalitis

2.1 Virology and epidemiology

Japanese Encephalitis (JE) is caused by the Japanese Encephalitis Virus (JEV), a mosquito-borne flavivirus. JEV is primarily transmitted by mosquitoes of the *Culex* genus, particularly *Culex tritaeniorhynchus*, and is endemic in many parts of Southeast Asia and the Western Pacific (Oliveira et al., 2018; Pearce et al., 2018). The virus is known for causing severe encephalitis in humans, with a high mortality rate and significant long-term neurological sequelae in survivors (Mulvey et al., 2021). Despite the availability of effective vaccines, JE remains a leading cause of viral encephalitis in Asia, particularly affecting children under 14 years old. The epidemiology of JE is complex, involving various environmental, ecological, and social determinants that influence its transmission and geographic spread.

2.2 Transmission cycle and primary vectors

The transmission cycle of JEV is intricate, involving multiple hosts and vectors. The primary vectors are mosquitoes of the *Culex* genus, with *Culex tritaeniorhynchus* being the most significant in many regions (Mulvey et al., 2021). Pigs serve as the main amplifying hosts, while ardeid birds, such as egrets and herons, act as natural reservoirs (Oliveira et al., 2018; Mulvey et al., 2021). During outbreaks, pigs play a crucial role in amplifying the virus, which is then transmitted to humans through mosquito bites (Figure 1) (Ladreyt et al., 2019; Mulvey et al., 2021). Human infection is considered a dead end in the virus's life cycle, as humans do not contribute to further transmission (Pearce et al., 2018). Other mosquito species, such as *Culex annulirostris*, *Culex quinquefasciatus*, and *Culex sitiens*, have also been identified as potential vectors, particularly in regions like Australia where JEV has recently emerged (Furlong et al., 2022; Hurk et al., 2022; Furlong et al., 2023).

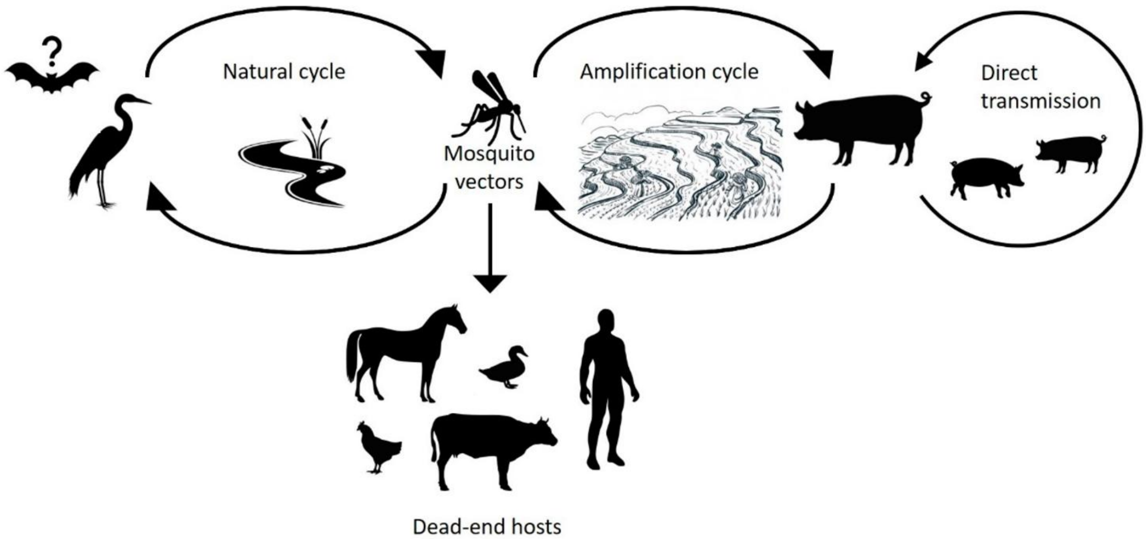

Figure 1 Overview of the Japanese encephalitis virus transmission cycle (Adopted from Mulvey et al., 2021)

2.3 Geographic distribution and affected populations

JE is predominantly found in Southeast Asia, the Western Pacific, and parts of the Pacific Islands. However, recent outbreaks in regions like southeastern Australia indicate an expanding geographic range, likely influenced by factors such as climate change, urbanization, and changes in agricultural practices (Pearce et al., 2018; Furlong et al., 2022; Hurk et al., 2022; Furlong et al., 2023). In Australia, the primary vectors include *Culex annulirostris* and *Culex sitiens*, with significant presence along the eastern and northern coastlines. The affected populations are primarily rural communities with close proximity to rice paddies, pig farms, and water bodies, which provide ideal breeding grounds for the mosquito vectors (Liu et al., 2018; Pearce et al., 2018; Furlong et al., 2023). Children are particularly vulnerable to JE, with the highest incidence rates observed in those under 14 years old. The disease's impact on human health underscores the need for increased surveillance, vaccination, and targeted vector control measures to mitigate the risk of JE transmission (Oliveira et al., 2018; Ladreyt et al., 2019; Mulvey et al., 2021).

3 Environmental Factors Affecting Transmission

3.1 Climate and weather patterns (temperature, rainfall, humidity)

Climate and weather patterns significantly influence the transmission dynamics of Japanese Encephalitis (JE). Temperature, rainfall, and humidity are critical factors that affect the development and survival of mosquito vectors, as well as the replication of the JE virus. Studies have shown that JE incidence is positively associated with higher temperatures and increased rainfall. For instance, a study in Southwestern China found that JE cases increased with daily average temperatures above 20°C and with higher daily rainfall, with a 25-day and 30-day lag, respectively. Similarly, research in Eastern Uttar Pradesh, India, indicated that increases in mean temperature, minimum temperature, rainfall, and relative humidity were associated with higher JE admissions and mortality. These findings underscore the importance of considering meteorological factors in JE prevention and control strategies, particularly in warm and rainy conditions (Yi et al., 2019; Liu et al., 2020; Singh et al., 2020).

3.2 Landscape and land use changes (agricultural practices, urbanization)

Landscape and land use changes, including agricultural practices and urbanization, play a crucial role in JE transmission. The presence of wetlands, rain-fed agriculture, and the density of domestic pigs and chickens are significant risk factors for JE outbreaks. A study in India highlighted that JE outbreak risk was strongly associated with landscapes that support wild ardeid birds and domestic pigs, particularly in fragmented rain-fed agricultural areas and wetlands. Additionally, urbanization has been found to inversely correlate with JE incidence, suggesting that rural areas with extensive agricultural activities are more prone to JE outbreaks. These findings emphasize the need for targeted public health interventions in high-risk landscapes to mitigate JE transmission (Zhang et al., 2018; Walsh et al., 2022).

3.3 Water bodies and irrigation practices

Water bodies and irrigation practices are critical environmental factors influencing JE transmission. Mosquito vectors, particularly *Culex* species, thrive in water-rich environments, which provide breeding grounds for their larvae. The presence of paddy fields, irrigated lands, and other water bodies has been identified as a significant risk factor for JE occurrence. Research in China demonstrated that JE cases were concentrated in areas with broad-leaved evergreen forests, shrubs, paddy fields, and irrigated lands, highlighting the role of these environments in supporting mosquito populations. Effective management of water bodies and irrigation practices is essential to reduce mosquito breeding sites and control JE transmission (Huang et al., 2018).

3.4 Seasonality and mosquito population dynamics

Seasonality and mosquito population dynamics are pivotal in the epidemiology of JE. The seasonal distribution of JE cases is closely linked to the population dynamics of mosquito vectors, which are influenced by climatic conditions. Studies have shown that JE incidence peaks during the monsoon season when temperature, rainfall, and humidity are optimal for mosquito breeding and virus transmission. For example, in Gorakhpur, India, temperature was significantly associated with JE during pre-monsoon and post-monsoon periods, while rainfall, relative humidity, solar radiation, and wind speed were associated with JE during the monsoon season (Singh et al., 2020). Additionally, the density of mosquito populations in livestock sheds has been found to affect JE outbreak risk, further illustrating the importance of understanding mosquito population dynamics in relation to seasonal changes (Tu et al., 2021). These insights are crucial for developing timely and effective JE control measures.

4 Ecological Factors Influencing JE Transmission

4.1 Host-vector interactions (humans, animals, and mosquitoes)

Japanese Encephalitis Virus (JEV) transmission is heavily influenced by interactions between hosts and vectors. The primary vectors of JEV are mosquitoes, particularly those in the *Culex* genus, such as *Culex tritaeniorhynchus* and *Culex annulirostris*, which are known for their high vector competence and capacity (Auerswald et al., 2021; Eynde et al., 2022). These mosquitoes feed on both pigs and birds, which are key amplifying hosts, thereby facilitating the virus's zoonotic cycle (Oliveira et al., 2018; Pearce et al., 2018; Hurk et al., 2022). Human infections occur when these mosquitoes feed on humans, who are considered dead-end hosts as they do not contribute to further transmission of the virus (Mulvey et al., 2021).

4.2 Mosquito breeding habitats and preferences

The breeding habitats of JEV vectors are crucial for understanding transmission dynamics. *Culex* mosquitoes, particularly *Culex tritaeniorhynchus*, prefer to breed in rice paddies, marshes, and other stagnant water bodies, which are abundant in many parts of Southeast Asia. These habitats provide ideal conditions for mosquito proliferation, especially during the monsoon season when water bodies are plentiful (Walsh et al., 2022). The presence of these breeding sites in close proximity to human dwellings and livestock farms increases the risk of JEV transmission (Pearce et al., 2018; Hurk et al., 2022).

4.3 Animal reservoirs and migration patterns

Pigs and wild ardeid birds, such as egrets and herons, are significant reservoirs for JEV. Pigs are particularly important as they develop high viremia levels, making them efficient amplifying hosts (Hurk et al., 2022). Wild birds also play a critical role in the virus's ecology, as they can carry the virus over long distances during migration, potentially introducing JEV to new areas (Mulvey et al., 2021; Hameed et al., 2022). The movement and density of these animal populations, therefore, have a direct impact on the spread and outbreak potential of JEV (Hameed et al., 2022; Walsh et al., 2022).

4.4 Changes in biodiversity and ecosystem health

Changes in biodiversity and ecosystem health can significantly influence JEV transmission. For instance, the loss of natural habitats and the creation of fragmented landscapes can alter the distribution and abundance of both vectors and hosts. Wetlands and rain-fed agricultural areas, which are often associated with high biodiversity, have been identified as high-risk landscapes for JEV outbreaks (Walsh et al., 2022). Additionally, climate change and urbanization can modify mosquito breeding sites and host availability, further affecting transmission dynamics. Increased surveillance and ecological studies are needed to better understand these complex interactions and to develop effective control strategies (Pearce et al., 2018; Faizah et al., 2020).

5 Case Study

5.1 Description of the selected location (region or country)

For this case study, we focus on the recent emergence of Japanese Encephalitis (JE) in Australia. Historically, JE has been predominantly confined to Southeast Asia, but recent outbreaks have highlighted its potential for geographic expansion (Williams et al., 2022; Kwa et al., 2023).

5.2 Local environmental and ecological characteristics

Australia's diverse climate and ecological zones provide a unique setting for the study of JE transmission. The country has a range of environments from tropical to temperate, which can influence mosquito populations and JE virus (JEV) transmission dynamics (Figure 2) (Hurk et al., 2022). Indigenous mosquito species, such as *Culex annulirostris*, have been identified as local vectors capable of transmitting JEV. Additionally, the presence of amplifying hosts like swine plays a crucial role in the local epidemiology of JE (Williams et al., 2022; Kwa et al., 2023).

Hurk et al. (2022) presents an analysis of host-feeding patterns of Australian *Culex* mosquito species, focusing on their role in the transmission of Japanese Encephalitis Virus (JEV). Blood meal data from 16 948 samples across 11 species were categorized into three climatic regions: equatorial and tropical, subtropical, and temperate. The figure highlights the varying proportions of blood meals derived from different vertebrate hosts, including birds, pigs, and humans, which are key to the JEV transmission cycle. Mosquitoes such as *Culex annulirostris* and *Culex quinquefasciatus* show significant feeding on humans and birds, especially in tropical regions, while other species like *Culex cylindricus* exhibit strong feeding on humans across regions. The variations in feeding behavior across species and regions indicate the diverse ecological roles mosquitoes play in JEV transmission. This research provides crucial insights into vector-host interactions and the potential risk of JEV outbreaks based on mosquito feeding patterns and regional climatic factors.

Figure 2 Identification of the vertebrate source of blood meals of Australian species of *Culex*, with a focus on animal groups of importance to Japanese encephalitis virus transmission cycles. Source data were from previously published studies (Adopted from Hurk et al., 2022)

5.3 JE transmission patterns and contributing factors

The transmission patterns of JE in Australia have shown a significant shift, with local transmission being reported for the first time in 2022. This unprecedented scale of transmission involved indigenous mosquitoes and amplifying swine hosts, leading to human infections (Williams et al., 2022). Several factors contribute to this pattern, including:

Climate Change: Warmer temperatures and increased rainfall can enhance mosquito breeding and virus transmission (Williams et al., 2022).

Ecological Drivers: The presence of suitable mosquito vectors and amplifying hosts in close proximity to human populations increases the risk of JE outbreaks (Williams et al., 2022; Kwa et al., 2023).

Human Activities: Urbanization and changes in land use can create new habitats for mosquitoes and bring humans into closer contact with vectors and hosts (Pearce et al., 2018; Song et al., 2020).

5.4 Lessons learned and implications for future research

The emergence of JE in Australia underscores the importance of continuous surveillance and adaptive public health strategies. Key lessons include:

Enhanced Surveillance: There is a need for robust surveillance systems to monitor mosquito populations and JEV activity, particularly in regions at risk of introduction and spread (Williams et al., 2022; Kwa et al., 2023).

Integrated Vector Management: Effective control of mosquito populations through environmental management and targeted interventions can reduce the risk of JE transmission (Pearce et al., 2018; Williams et al., 2022).

Vaccination Programs: Expanding vaccination coverage, especially in at-risk areas, can significantly reduce the incidence of JE (Moore, 2021; Srivastava et al., 2023).

Climate and Ecological Research: Further studies on the impact of climate change and ecological factors on JE transmission are essential to predict and mitigate future outbreaks (Song et al., 2020).

6 Control and Prevention Strategies

6.1 Environmental management and vector control measures

Environmental management and vector control are critical components in the fight against Japanese Encephalitis (JE). The primary vector for JE is the *Culex* mosquito, particularly *Culex tritaeniorhynchus*, which thrives in rice paddies and other stagnant water bodies common in rural Asia. Effective vector control strategies include the reduction of mosquito breeding sites through environmental management, such as improved water management and sanitation practices (Pearce et al., 2018). Additionally, the use of insecticides and larvicides can help reduce mosquito populations. However, these measures must be carefully managed to avoid ecological disruption and the development of insecticide resistance. Integrated vector management, combining environmental management with chemical and biological control methods, has shown promise in reducing JE transmission (Diallo et al., 2018).

6.2 Vaccination programs and public health initiatives

Vaccination remains the cornerstone of JE prevention. Several vaccines are available, including the live-attenuated SA 14-14-2 vaccine and the inactivated Vero cell-derived vaccine (IC51). These vaccines have demonstrated high efficacy and safety profiles, with seroprotection rates ranging from 91% to 100% in various populations (Kling et al., 2020). Public health initiatives have focused on incorporating JE vaccination into national immunization programs, particularly in endemic regions. The support from organizations like Gavi has been instrumental in increasing vaccine coverage and reducing JE incidence (Quan et al., 2019). For travelers to endemic areas, vaccination is recommended, although acceptance rates remain low due to cost and perceived risk. Public health campaigns aimed at increasing awareness and accessibility of JE vaccines are essential to improving vaccination rates (Vannice et al., 2021; Asawapaithulsert et al., 2023).

6.3 Challenges and opportunities in implementing control measures

Implementing JE control measures faces several challenges. One significant challenge is the variability in JE epidemiology across different regions, which necessitates tailored control strategies (Ladreyt et al., 2019). Additionally, the high cost of vaccines and logistical difficulties in reaching remote populations hinder widespread vaccination efforts (Srivastava et al., 2023). There is also the issue of vaccine hesitancy and low acceptance rates among travelers and local populations (Asawapaithulsert et al., 2023). However, opportunities exist to enhance JE control. The development of cost-effective vaccines, such as the CD-JEV live-attenuated vaccine, offers a promising solution to reduce financial barriers (Sakamoto et al., 2019). Furthermore, combining human vaccination with vector control and pig vaccination can provide a more comprehensive approach to reducing JE transmission (Diallo et al., 2018). Strengthening surveillance systems and improving diagnostic capabilities are also crucial for timely detection and response to JE outbreaks (Pearce et al., 2018).

6.4 Role of predictive modeling in planning interventions

Predictive modeling plays a vital role in planning and optimizing JE control interventions. Models can simulate various scenarios to assess the impact of different control measures, such as vector control, pig vaccination, and human vaccination, on JE transmission dynamics. These models help identify the most effective strategies and allocate resources efficiently. For instance, a deterministic metapopulation model has been used to evaluate the combined effects of sow vaccination, vector control, and pig herd management on JE transmission, highlighting the potential benefits of integrated control measures (Diallo et al., 2018). Predictive models also aid in understanding the influence of environmental factors, such as climate change and urbanization, on JE epidemiology, thereby informing adaptive strategies to mitigate future risks (Pearce et al., 2018). By incorporating data on vector competence, genetic variation, and environmental conditions, predictive models provide valuable insights for targeted and evidence-based JE control efforts (Oliveira et al., 2018).

7 Future Directions and Research Needs

7.1 Gaps in current knowledge

Despite significant advancements in understanding Japanese Encephalitis (JE), several gaps remain that hinder effective control and prevention strategies. One major gap is the limited understanding of the role of secondary vectors and hosts in JE transmission. While pigs are well-established as primary amplifying hosts, the potential involvement of other animals such as feral pigs, poultry, and dogs needs further investigation (Ladreyt et al., 2019; Oliveira et al., 2020; Ladreyt et al., 2022). Additionally, the genetic variation of the JE Virus (JEV) and its impact on transmission dynamics and disease severity is not fully understood, necessitating more comprehensive genetic studies (Pearce et al., 2018). Another critical gap is the lack of effective antiviral treatments and the limited use of available vaccines due to high costs and side effects, which restricts their global application (Srivastava et al., 2023). Furthermore, the diagnostic procedures for JE are often inadequate, with many cases confirmed using low-confidence tests, highlighting the need for more reliable and accessible diagnostic tools (Bharucha et al., 2020).

7.2 Emerging trends in JE transmission

Recent trends indicate a potential expansion of JE beyond its traditional geographic confines, driven by factors such as climate change, urbanization, and changes in agricultural practices (Pearce et al., 2018; Mackenzie et al., 2020; Mulvey et al., 2021). For instance, the emergence of JEV genotype IV in Australia and its potential for endemicity underscores the virus's ability to adapt to new ecological niches. Meteorological factors, including temperature and rainfall, have been shown to significantly influence JE transmission, with warmer and wetter conditions increasing the risk of outbreaks (Liu et al., 2020; Tu et al., 2021). Additionally, the role of feral pigs and other wildlife in the spread of JEV in non-endemic regions, such as the United States, is gaining attention, suggesting that these animals could facilitate the virus's introduction and establishment in new areas (Oliveira et al., 2020).

7.3 Recommendations for future studies

To address these gaps and emerging trends, future research should focus on several key areas. First, long-term longitudinal studies are needed to monitor vector populations and their competencies, particularly in relation to secondary vectors like *Culex pipiens* and *Culex bitaeniorhynchus*, to better understand their roles in JE transmission (Pearce et al., 2018). Second, genetic studies should be expanded to explore the diversity of JEV strains and their implications for disease epidemiology and vaccine development (Pearce et al., 2018). Third, there is a pressing need to develop cost-effective and side-effect-free antiviral treatments and vaccines to enhance global JE control efforts (Srivastava et al., 2023). Fourth, improving diagnostic tools to provide rapid, accurate, and accessible testing in endemic regions is crucial for timely disease management (Bharucha et al., 2020). Lastly, incorporating environmental and ecological data into predictive models can help identify high-risk periods and areas, enabling more targeted and effective intervention strategies (Liu et al., 2020; Mulvey et al., 2021; Tu et al., 2021). By addressing these research needs, we can better understand and mitigate the factors influencing JE transmission, ultimately reducing the disease burden globally.

Acknowledgments

We would like to thank Dr. Li for the assistance and support during the research process, which contributed to the completion of this paper.

Conflict of Interest Disclosure

Authors affirm that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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