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Review Article

Urban Japanese Encephalitis: Time for a Reality Check

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A B S T R A C T

Expansion of JEV from its historical rural origin in the Oriental Realm has been evident. Apprehensions were raised by several investigators that the occurrence of Japanese Encephalitis (JE) in the urban areas is a possibility. Creating wetlands, rice farms, and piggeries close to the rural-urban periphery to support the increasing urban population facilitates the migration of mosquitoes, ardeid birds, and pigs in these areas. The presence of vectors (*Culex vishnui* complex), reservoirs (the ardeid birds), and the amplifying hosts (pigs) together in these urban and peri-urban areas creates highly conducive situations for the JE transmission thus, creating an urban ecotype for JE. Apart from the primary vectors, JEV has been isolated from several species of mosquitoes belonging to different genera. JE antibodies have also been detected in several birds and mammals other than the known reservoirs and amplifying hosts. Such mosquitoes, birds, and mammals might be acting as complementary or maintenance vectors and reservoirs, respectively, which likely can keep the virus circulating perennially in nature. The reported occurrence of JE in urban areas from different geographical locations is decidedly indicative of the reality of the urban JE. It is thus pertinent that an inclusive approach encompassing sustained epidemiological surveillance and monitoring be adopted to formulate season-wise and area-wise strategies to contain JE both in rural and urban areas.

Keywords: Japanese Encephalitis, Virus, Vector, Reservoir, Urban Areas

Introduction

Japanese Encephalitis (JE) is a vector-borne viral zoonosis caused by the Japanese Encephalitis Virus (JEV) belonging to the family Flaviviridae.[1] It is estimated that, around the world, nearly 68000 clinical JE cases occur, with about 13000 to 20000 deaths every year.[2] The transmission cycle of JEV involves ardeid birds, Culex mosquitoes, pigs functioning as principal reservoirs, primary vectors, and amplification hosts respectively that keep the virus circulating in nature.[3] The risk of JE is associated with rural residents living close to the rice fields and pig-rearing places.[4] The rice fields in rural areas serve as breeding and larval developmental sites for the vectors of JE such as *Culex tritaeniorhynchus*, and eventually contribute to the disease ecology.[5] Rapid urbanization to sustain the swelling urban population, changes in land-use patterns for urban agriculture, urban housing, industries, pasture, and the establishment of urban

water bodies coupled with a continuous 'urban pull' or 'rural push' has impacted the epidemiology of JE.[6] In such changing environmental situations, apprehensions have been raised that JE in urban areas might be a "possibility" expanding its reach from its traditional rural origin.[6] In this context, this review is an attempt to assess and analyze the ground reality of the prevalence of urban JE ecotype, if any.

Methodology

Research studies were drawn from literature searches targeted peer-reviewed journal articles to conduct an exploratory review. The databases were used for data search during the study are PubMed, Google Scholar, and Wiley Online Library. These databases represent a range of disciplines allied to Japanese Encephalitis, Urbanization, Zoonoses, and Vector-borne diseases. The findings and observations regarding the focused topics in this review are listed in the references section accordingly.

Urban JE Scenario

There have been reports of JE case incidences in urban areas of different parts of the world by several investigators. In major cities like Kolkata (India), Delhi (India), Rourkela (India) and Dhaka (Bangladesh) (Table 1), JE cases have been reported in different periods, although they were sporadic. In urban areas of Delhi, all the patients of JE had no history of rural travel, which strongly indicates a possible local JEV transmission cycle.[4] Presence of JE vectors - *Cx. tritaeniorhynchus* and *Cx. vishnui* with the reservoir hosts of JEV in this area further lends support to this assumption.[4] Vajpayee A et al. have reported JE cases in Rourkela city (Orissa) and the presence of pigs in these JE-affected areas.[7] Later a study by Dash AP et al. from the urban area of Rourkela reported the presence of the JE vector, the *Culex vishnui* subgroup, along with JE cases.[8] Sporadic case incidences of JE from Kolkata have also been reported by several investigators.[9,10] Bhattacharya S, Santra SC have reported the presence of *Cx. vishnui* and *Cx. quinquefasciatus*, the vectors of JE in India in the urban periphery of Kolkata.[11] The peri-urban regions of Kolkata have a sizable population of pigs - the reservoir and amplifying host of JEV. Ardeid birds are also present near the water-bodies of Kolkata.[12] JE vectors, reservoir hosts, and amplifying hosts (pigs) were also reported from the urban and urban periphery of many cities globally viz. Shanghai (China), Lianyungang City (China), Can Tho City (Vietnam), and Phnom Penh (Cambodia) (Table 1). However, no JE cases have so far been reported from all these above mentioned four urban areas (Table 1). Nonetheless, these JE vectors and reservoir hosts in the aforesaid areas create highly conducive environments to support the JE transmission dynamics.

Table 1.JEV Vectors, Reservoirs and Case incidences in Urban/ Peri-urban areas

Urban/ Peri-Urban Area	Vector or Suspected Vectors of JEV	Reservoir Hosts of JEV in Urban or Per-urban Areas	JE Case Incidences		References
			Cases	Year	
National Capital Territory of Delhi, India	*Cx. vishnui, Cx. pseudovishnui, Cx. tritaeniorhynchus*	Pigs were present and found positive for JEV antibodies	4	2013	Kumari R et al.[4]
Rourkela, Orissa, India	*Cx. vishnui, Cx. pseudovishnui, Cx. tritaeniorhynchus*	Pigs were present in JEV affected areas	41	1989	Vajpayee A et al.[7] Dash AP et al.[8]
Kolkata, West Bengal, India	*Cx. vishnui, Cx. quinquefasciatus*	The ardeid birds were present in Kolkata	12	2007-2012	Taraphdar D et al.[9] Chakraborty D et al.[10] Chakraborty DC, Majumdar S[11] Bhattacharya S, Santra SC[12]
Dhaka city, Bangladesh	*Cx. vishnui, Cx. gelidus, Cx. tritaeniorhynchus*	Not reported	3	2003	Khan RH et al.[13] Hossain MJ et al.[14]
Shanghai, China	*Cx. tritaeniorhynchus, Cx. pipiens*	Not Reported	Not Reported		Fang Y et al.[15]
Can Tho City, Vietnam	*Cx. vishnui, Cx. gelidus, Cx. tritaeniorhynchus*	Pig farming in the urban periphery	Not Reported		Lindahl J et al.[16]

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Phnom Penh, Cambodia	*Cx. vishnui, Cx. gelidus, Cx. tritaeniorhynchus*	Sentinel pig population in peri-urban areas	Not Reported		Di Francesco J et al.[17]
Lianyungang City, Jiangsu province, China	*Cx. tritaeniorhynchus*	JEV isolated from the pigs	Not Reported		Chu H et al.[18]

Vectors and suspected vectors of JE

JEV primarily gets transmitted by the mosquitoes belonging to Culex vishnui subgroup constituted by *Cx. tritaeniorhynchus*, *Cx. vishnui* and *Cx. pseudovishnui*.[4,19,20] In addition to the confirmed primary vectors of JE, the Culex vishnui subgroup, several other mosquitoes belonging to different genera were assumed to be contributing to the epidemiology of JEV as complementary or secondary vectors following the isolation of the virus from them. *Cx. annulirostris*, *Cx. annulus*, *Cx. fuscocephala*, *Cx. gelidus*, and *Cx. sitiens* are the most cited competent vectors apart from the *Cx. vishnui* subgroup within the Culex genus.[21] Scientists have speculated that *An. subpictus* could contribute to the epidemiology of JE owing to their presence in high numbers during JE epidemics in certain parts of India.[22,23] Isolation of JEV from other commonly encountered mosquito species viz. *An. peditaeniatus*, *An. barbirostris* and *An. pallidus* has been reported.[23,24] The vectorial competence of *Ae. Albopictus*, *Ae japonicas*, and *Ae. Detritus* mosquitoes also were demonstrated by investigators.[25-27] Among these mosquitoes, *Ae. albopictus* as a contributor to the transmission dynamics of JEV could be significant due to its wide home-range and anthropo-zoophilic feeding behavior.[19] JEV was isolated from mosquitoes belonging to genera Mansonia and Armigeres also.[28] However, the role of these mosquitoes as complementary vectors for JEV, if any, has not been established as yet. Further studies are required to determine their possible impact on the epidemiology of the disease.

Vertebrate Reservoirs and Amplifier Hosts of JE

The transmission dynamics of JEV primarily involve birds, mosquitoes and swine.[3] Several paddy field birds belonging to the family Ardeidae viz. the egrets, herons, cranes are the principal reservoir hosts of JEV.[29] Domestic birds such as chickens, ducks, and pigeons were apprehended as possible reservoir hosts for JEV as they had attained reasonably good level of blood viremia during experimental investigation.[22] Besides that, pigs are primarily considered the principal amplifying host of JE in the endemic areas.[30,4] The intra-specific transmission of JEV via nasal secretions of pigs without mosquito vectors has also been reported and could be a significant component in its disease epidemiology.[31] Isolation of JEV from bats has been evident, but their role as the reservoir for the virus needs further investigation.[32] The isolation of JEV from some poikilothermic reptiles like snakes and freshwater turtles has also been reported.[33,34]

Impact of Urbanization, Land-use Change, and Deforestation on the Ecology of JE

Rapid urbanization is a reason behind the changing epidemiology of several vector-borne zoonoses.[16] To sustain the growing demands of the urban population, land-use changes in the form of the creation of new agricultural lands, water bodies could significantly moderate the disease dynamics of JEV.[16] The establishment of water bodies provides the ideal breeding ground for mosquitoes such as *Cx. tritaeniorhynchus*, which are traditionally prevalent in rural rice cultivating areas and act as primary vectors for JE.[5] The destruction of habitats of the avian reservoir hosts such as ardeid birds forces them to find new habitats for foraging and breeding in the modified lands such as urban or peri-urban water bodies, which brings them in close proximity to humans.[35] The livestock rearing in peri-urban areas also tends to modify the host range of the JEV.[36] Domestic pig rearing is a risk factor for JEV transmission to humans, as infected pigs are the main amplifying hosts for JEV.[37] Lindahl J et al. provided evidence of increased density of *Cx. vishnui* complex mosquitoes in urban areas where pig-rearing was being undertaken.[16] It emphasizes the role of pig farming as a contributor in likely urban JE transmission.

Discussion

Historically, JE has been endemic in the rural regions of the Oriental realm as the cause of mosquito-borne viral encephalitis. Evidence of the introduction of JEV into Northern Australia from a source in Papua New Guinea confirms its expansion into newer geographical areas.[38] Climate change and global warming have been delineated as supporting factors for the expansion of vector-borne zoonoses by several authors.[39,40] In warmer temperatures, female mosquitoes tend to have blood meals more frequently.[40] Moreover, the vector density also increases in a warmer climate with increased breeding and the ability to invade higher altitudes for vector mosquitoes.[40] Rapid urbanization, deforestation, globalization, industrialization, construction and irrigation has changed the environmental conditions in rural and urban habitats of the vectors, reservoirs and hosts for several diseases.[41] These changes could also act as a driver

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for the spread of JEV in newer areas. Expansion of cities to accommodate the growing urban population has led to the urban boundaries coming closer to the rural stretches. Eventually, to sustain the swelling urban population, urban forestry and urban water-bodies are being created, giving rise to novel urban ecosystems. As a result, the prevalence of wading water birds like storks, herons, egrets inhabiting these urban water-bodies are rising, thereby introducing possible new reservoirs of JEV in urban areas.[12,42] These wetlands additionally provide breeding grounds for mosquitoes to sustain themselves in urban conditions.[19] The isolation of JEV from certain species of genus Anopheles, Mansonia, Aedes, and Culex mosquitoes, apart from their primary vectors, the *Culex vishnui* subgroup, has been well demonstrated. However, virus isolation from these mosquitoes is not enough to confirm their vectorial status and needs further investigations to prove their decisive role in JE transmission. These mosquitoes could play a significant role as possible complementary or maintenance vectors for JEV and with the passage of time, may attain the status of vectors.[1] It is well-established that the diverse feeding habits of principal and complementary vectors can facilitate the virus to circulate perennially in nature.[43] The growing food demand of the expanding urban communities met through livestock (cattle farming) rearing along with rice farming and the creation of piggeries in the peri-urban areas has led to an abundance of pigs -the amplifier host of JEV thereby, enhancing the risk of JE transmission in these areas.[6] The possibility of enzootic cycles of JEV to exist in such mosquitogenic and virogenic environments is highly probable. Involvement of the young, non-immune pigs, nestling birds, and other mammalian populations in the transmission dynamics of JEV could facilitate and transform the enzootic cycle into the epizootic cycle.[44,45,50] It is highly likely that during the increased viral load in these animals, JEV may tangentially spillover to humans.[1] Bhattacharya S et al. showed that the JEV antibodies were prevalent in wild birds and sentinel chicks perennially, and when the average level of virus circulation increases human infection happens periodically that is, at the peak of the epizootic cycle.[44] Antibodies against JEV have also been detected from several animals apart from the known reservoirs, the ardeid birds and pigs, which have added a new dimension in the epidemiology of JE. Among these animals, ducks, chicken, pigeons, bats are commonly present in urban and peri-urban areas. However, the detection of JE antibody is not enough to attain the status of the reservoir for JE, but with the passage of time, these animals could be epidemiologically important and could play the role of complementary or secondary reservoirs/hosts by helping the virus to sustain during the enzootic cycle in urban environments.[1] Further experimental studies are required to understand the contribution of these complementary hosts in the transmission dynamics of JEV. Moreover, mosquitoes prevalent in rural-urban eco-epidemiological zones, such as *Culex quinquefasciatus*, could also act as an ecological bridge vector between urban, peri-urban, and rural areas as well as a bridge vector between human, pigs, and birds owing to their distribution and diverse feeding habits.[46,47] Isolation of JEV from *Culex quinquefasciatus* has been documented by investigators.[48]

Lindahl J had apprehended the "possibility" of an urban JE.[6] The case incidences of JE in cities such as Delhi (India) and Katmandu (Nepal) without any rural travel history are significant and hint towards the probable urban indigenous transmission cycle of JE.[4,6,49] This scenario reinforces the existence of an urban ecotype for JEV, thus, making urban JE seems reality now. However, the magnitude of the urban JE appears to be minuscule at present. It is thus extremely important and imperative necessity that in all urban areas where JE disease ecology is prevalent with the recorded presence of vectors, reservoir hosts, and susceptible populations, thorough investigations need to be prioritized and strategies formulated to avert the urban JE outbreaks, if any.

Conclusion

The transmission dynamics of vector-borne viral zoonosis are complex, with several components. The changing disease ecology of vector-borne diseases due to several anthropogenic and environmental factors facilitates their spread to newer areas. Urbanization and subsequent land-use changes create favorable situations for the transmission and maintenance of JEV in the urban and suburban periphery. The prevalence of JE vectors, reservoir hosts, with JE incidences in certain urban areas indicates the reality of the existence of urban JE ecotype. Sustained surveillance and thorough monitoring of vector, virus, and vertebrate reservoir hosts in urban areas are required to prevent any possible future outbreaks of urban JE.

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