

Potential for the Invasive Species *Aedes Albopictus* and Arboviral Transmission through the Chabahar Port in Iran

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What's Known

- Previous studies and modeling of the suitability for the global distribution of *Aedes aegypti*, *Aedes albopictus* and the arbovirus species they transmit are often of low resolution (about 5 km²).
- These published models sometimes produce contradictory results.

What's New

- A predictive output model for *Aedes* species and arboviruses at high resolution (up to 30 m²) is provided.
- BioTEMS provides medical and public health officials a probable directional movement of invasive mosquito species, identifies zones where mosquito control should be prioritized, and identifies sites for human and vector epidemiologic surveillance.

Abstract

Background: Dengue, chikungunya, and Zika viruses are emerging infectious disease threats wherever suitable vectors, hosts, and habitat are present. The aim of the present study was to use the bioagent transport and environmental modeling system (BioTEMS) to identify the potential for arbovirus-infected *Aedes* species to invade the Chabahar area in southeastern Iran.

Methods: ArcGIS geospatial analysis software, Statistica software, and BioTEMS were used to analyze geographic information and conduct data analysis. BioTEMS utilizes up to several hundred abiotic and biotic factors to produce risk and vulnerability assessments for biological agents and infectious diseases. The output of BioTEMS was validated using published predictive models, and most importantly published collection data of *Aedes* species in Iran.

Results: There appears to have been two separate invasion events by *Ae. albopictus* into the southern region of Iran, first preceding 2009 and then again in 2013. BioTEMS identified two probable areas of introduction during the 2009 time frame, either through one or both the Chabahar ports or the Iranshahr airport with subsequent spread through vehicular transport. BioTEMS identified the port as an introduction zone for ZIKAV with high-risk zones and identifies gap zones during the 2013 time frame. Recommended surveillance sites are provided.

Conclusion: The air and maritime ports of Iran serve international customers, and are therefore vulnerable to import and invasion of mosquito vectors and arboviruses. Based on comparisons with other published low-resolution models, BioTEMS provides information for medical and public health professionals conducting integrated mosquito management, preventive medicine, and epidemiological surveillance.

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Introduction

Mosquitoes and the pathogens they transmit can have a significant impact on the health and economy of a community. In the Islamic Republic of Iran, several arboviruses and malaria are endemic; non-human filariasis has been documented, but the status of human filariasis in Iran is unclear.^{1,2} Doosti et al. (2016) stated, "epidemics of mosquito-borne viral infections such as

dengue, chikungunya, West Nile, and Rift Valley fevers in neighboring countries and the risk of introduction of exotic vectors into Iran have placed this country at a significant risk for these mosquito-borne diseases.³ In the southeastern region of Iran, West Nile virus is present and the possibility for the introduction of Rift Valley fever (RVFV) remains a concern.^{4,5} Zika virus (ZIKAV) is invading globally where competent vectors, hosts, and habitats occur. ZIKAV is the most recent arbovirus put into status as a public health emergency by the World Health Organization; it has recently been removed as a public health emergency of international concern, but remains a significant and long-term public health problem.⁶

ZIKAV was first isolated in 1947 from a rhesus macaque monkey and in 1948 from *Aedes africanus* from cages placed on a tower in the Zika forest near Lake Victoria, Uganda.⁷ ZIKAV is no longer restricted to transmission by *Ae. africanus* in the tropical forest ecosystem in Africa. Several *Aedes* species, including *Ae. albopictus*, have been implicated in the transmission of ZIKAV to humans in urban habitats where the poor are particularly at risk.⁸ Sixty-one mosquito species have been recorded in Iran with no recent records of *Ae. aegypti*; *Ae. albopictus* was recently recorded in Iran in the Chabahar area in 2009.³ *Aedes albopictus* is one of the most medically important mosquito because of the number of pathogens it may transmit and its status as the most invasive mosquito species in the world. Twenty-six viruses have been associated with *Ae. albopictus*, and it is a viable vector of DENV, CHIKV, and ZIKAV.⁹⁻¹¹ Assessing the risk of invasion and implementation of integrated mosquito management (IMM), at the local level is critical in protecting communities from medically important vectors. Where *Ae. albopictus* has already invaded, immigration of susceptible and infected haplotypes should be of concern. For example, risk modeling of invasive mosquito species in the United Arab Emirates indicates the port of Dubai is vulnerable to invasion by *Ae. albopictus* and *Ae. vexans*.¹²

Like the UAE, the ports of Chabahar and surrounding areas in southeastern Iran may also be susceptible to invasion by *Ae. albopictus*. Medical and public health officials at the local level in Chabahar and elsewhere in Iran would benefit from high-resolution models, maps, and information concerning sites of possible invasion of mosquitoes infected with arboviruses. Once introduced into an area, the invasive mosquito species can spread rapidly across regions through ground transport.^{13,14} In addition to the import of infected mosquitoes, introduction of

arboviruses into a new geographic area can occur when local mosquitoes bite infected travelers and become infected, or when people become infected through sex or contaminated blood.^{15,16}

The air and maritime ports of Iran serve international customers and are therefore at risk for the introduction of mosquito vectors and arboviruses, as well as other infectious diseases. The Bioagent transport and environmental modeling system (BioTEMS) was used to model the potential for *Ae. albopictus* and arboviruses to enter the region through the Chabahar port area spread into Chabahar County and Sistan-Baluchistan Province. Identifying probable invasive mosquitoes and developing an IMM plan for communities is essential. BioTEMS output identifying recommended IMM zones, control methods, and surveillance sites is discussed in order to provide practical information to local medical and public health professionals.

Materials and Methods

The maritime port of Chabahar was evaluated for invasion by *Ae. albopictus*. Areas at risk of arboviruses and IMM zones were developed based on the BioTEMS TIGER model should an arbovirus be introduced through the port. ArcGIS geospatial analysis software, Statistica software, and BioTEMS were used to analyze geographic information and conduct data analysis. BioTEMS has previously been used for modeling biological weapons defense and infectious diseases in several countries.¹⁷ BioTEMS utilizes up to several hundred abiotic and biotic factors to produce risk and vulnerability assessments for biological agents and infectious diseases. Examples of biotic and abiotic factors include pathogen strain, vector/host relationship, vectorial capacity, host/vector physiology, colonization ability, population dynamics of hosts and vectors, soil, shade, and weather conditions, such as wind, temperature, precipitation, shade. Analytical methods within BioTEMS include artificial intelligence, fuzzy logic, niche analysis, and general additive regression.

Ecological niche and dynamic change modeling are often used to predict the potential for invasive species.^{18,19} Ecological niche and dynamic change modeling are used within BioTEMS to identify areas at risk for invasion by arboviruses and provide information for integrated mosquito management. The BioTEMS TIGER model has been used in several countries, e.g. Bangladesh, Brazil, Honduras, United Arab Emirates, and United States to assist in the identification of areas at high risk for

invasive mosquito species and mosquito-borne disease, optimize surveillance, and treatment zones.^{12,20-22} The acronym TIGER represents the six stages in the invasion of a mosquito species or haplotype:¹²

- Transport: Identifies the point of origin, method, and rate of transport to a locality.
- Introduction: The point or area of initial introduction/immigration of species or haplotypes and preliminary spread into a locality.
- Gap: Determines the area where vector/pathogen infiltrates and initially spreads once it has gained a foothold.
- Escalade: Incorporates abiotic and biotic factors as possible resistance to invasion.
- Residence and recruitment: Incorporates factors and area where vector/pathogen adds to genetic diversity or becomes endemic and recruits con-specifics/haplotypes.

The output from BioTEMS was compared to collection information of *Ae. aegypti* and *Ae. albopictus* in Iran and to global predictive maps.^{3,23-28} BioTEMS and ArcGIS were used to produce output into Google® Earth.

Results

The BioTEMS TIGER model predicted the suitability for the invasion of arbovirus-infected *Ae. albopictus* into southern Iran (figure 1). There appears to have been two separate invasion events by *Ae. albopictus* into the southern region of Iran, first in 2009 and then 2013. BioTEMS identified two probable areas of introduction into the region during 2009, through either or both the Chabahar ports or the Iranshahr airport with subsequent spread through vehicular transport (figure 1). BioTEMS identified the port as an introduction zone for ZIKAV with high-risk zones and identifies gap zones during the 2013 time frame (figure 2). High-risk zones are defined as an area likely to be invaded or have already been invaded by infected mosquitoes or to have localized transmission. The gap zone includes areas where ZIKAV will spread through infected mosquitoes. Recommended surveillance sites in the Chabahar and Ramin ports, Chabahar and along Highway 95 are provided (figure 2).

Discussion

The principal factor responsible for the invasion of disease vectors is through air and ship transport.^{29,30} Various models have been developed in order to identify and better understand the bionomics, treatment, epidemiology, and potential for geographic spread of ZIKAV. For example, A129

mice may provide an urgently required small animal model for testing of antivirals and vaccines because they are highly susceptible to infection by ZIKAV.³¹ Modeling sexual transmission and migration of humans demonstrated that sexual transmission influences the magnitude of an outbreak and migration influences the magnitude over time.³² When projecting the number of infections among childbearing women, Perkins et al. (2016) cautioned that a number of conditions would affect whether a local epidemic will take place such as; dispersal limitation, stochastic fadeout, and mismatches in geographic seasonality.³³ Several *Aedes* species have been implicated in the transmission of ZIKAV, e.g. *Ae. aegypti*, *Ae. albopictus*, *Ae. africanus*, *Ae. luteocephalus*, *Ae. vitattus*, *Ae. furcifer*, *Ae. Hensilli*, *Ae. apicoargenteus*, *Ae. polynesiensis*, and *Ae. taylori*.³⁴⁻⁴⁰ However, ZIKAV models of mosquito vectors have focused on the two primary and globally distributed vectors; *Ae. aegypti* and *Ae. albopictus*.^{13,41}

Most geographic models of low-resolution are valuable for ascertaining the current and potential geographic range of vector species and the pathogens they transmit, e.g. the 5 km² resolution maps for *Ae. aegypti* and *Ae. albopictus*.^{25,27,28,33} Low-resolution models (>1 km²) have limited utility for IMM and control efforts at the community level. There are various and contradictory conclusions drawn from published predictive global models of *Aedes* and arboviruses. Messina et al. (2016) categorized the entire country of Iran as having limited suitability for ZIKAV; however, Carlson et al. (2016) identified geographic variation in suitability for ZIKAV in Iran.^{25,27} BioTEMS supports the geographic variation in susceptibility proposed by Carlson et al. (2016) and the suitability of the environment and vector availability for ZIKAV in southeastern Iran proposed by Samy et al. (2016).^{25,28} The validity of the BioTEMS model for predicting the presence and spread of *Ae. albopictus* in southeastern Iran was also confirmed by the collection records of both adult and larvae stages of *Ae. albopictus*.³ In the Chabahar area, Kraemer et al. (2015) identifies the area as suitable for *Ae. aegypti*, which is a vector of ZIKAV; however, they did not predict the presence of *Ae. albopictus*.²⁶ It is possible that *Ae. aegypti* was indeed previously found in the Chabahar area, but when faced with invasion and competition by *Ae. albopictus*, *Ae. aegypti* is often eradicated or numbers significantly reduced.⁴² The BioTEMS model also fell within the combined global model of *Ae. aegypti*, *Ae. africanus*, and *Ae. albopictus* of Carlson et al. (2106) for the Chabahar region (figure 1).



Figure 1: Sites where *Aedes albopictus* has been reported in southeastern Iran in pink balloon (Doosti et al., 2016) with maritime ports and airports shown. Blue outline is the predicted area of ZIKAV excerpted from Carlson et al. (2016). Ship and plane symbols represent BioTEMS predicted areas of invasion by *Aedes albopictus* into southeastern Iran. Black arrow indicates BioTEMS primary direction of spread of *Aedes albopictus* if introduced through the maritime ports or airports in Chabahar.



Figure 2: Introduction zones (red) and gap zone (yellow) surrounding Chabahar City where surveillance and control efforts should be prioritized. Blue circles represent recommended surveillance sites. Sites where *Aedes albopictus* were collected in 2013 are shown in purple (Doosti et al. 2016).

When validated against several models, and more importantly local capture of *Aedes* vectors of ZIKAV, the high resolution of BioTEMS (often less than 30 m²) provides several features; e.g. 1) Point/area of invasion, 2) Identifying risk zones for prioritizing control and epidemiologic surveys, 3) Sites for surveillance efforts, and 4) Identifying where the infected invasive mosquitoes will most likely spread (figure 2). These features are not available in other lower resolution models. Using high-resolution models in IMM can greatly reduce the cost of pesticides and labor as well as reduce the risk to community health and environmental impact resulting from pesticide application.

After invasion, one of the principal routes of spread of *Aedes* species across a region is through vehicular transport.⁴³ The Kraemer model identifies the Chabahar area as suitable for *Ae. aegypti* but not *Ae. albopictus*.²⁶ However, recent mosquito surveys have only detected *Ae. albopictus* and not *Ae. aegypti* in the Chabahar area.⁴⁴ In previous studies, BioTEMS was accurate in predicting the presence of ZIKAV cases in Brazil and the USA through the import of infected *Aedes* species and infection of local mosquitoes.^{21,22} ZIKAV is primarily introduced into a new geographic area through an infected human traveler or by invasion of an infected mosquito. There is sometimes the failure of public health officials to recognize these two possibilities. For example, in a recent CBS 60 Minutes broadcast, Dr. Anthony Fauci (the head of infectious diseases at the U.S. National Institutes of Health) stated, "The mosquito did not fly from Rio de Janeiro to Florida. The mosquito flies 500 feet in a lifetime. It is the people who travel."⁴⁵ Ignoring the possibility of invasive mosquitoes in the contribution to the spread of mosquito-borne diseases ignores hundreds of years of evidence for vector mosquitoes being introduced into new geographic areas. *Aedes albopictus* is probably the most successful invasive mosquito species and it has been rapidly spreading globally, primarily through the trade in tires and lucky bamboo, arriving by ship and then spreading along highways.⁴³ Seaports play a critical role in the invasion of *Aedes* species, this includes recruitment of new haplotypes.⁴⁶ Both maritime ports and airports are important routes of invasion of mosquitoes infected with arboviruses.⁴⁷ Focusing control and surveillance efforts primarily on travelers and not including ports of entry do a disservice to the population to whom public health officials are charged to protect. For example, if Miami and Rio de Janeiro had an active ZIKAV surveillance system in place for mosquitoes in the port areas,

the chance of finding an infected mosquito would have been increased and IMM could have been initiated sooner.

As part of IMM, education of the local population on reducing breeding sites by emptying containers and the use of personal protective measures can greatly reduce the risk of mosquito-borne infections. These include; personal protection by using repellents, daytime avoidance of mosquito bites for pregnant mothers and ZIKAV infected patients, and community-level surveillance and control measures.⁴⁸ Previously published models provide little information with which local medical and public health officials can incorporate in their IMM strategy and planning beyond only recognizing that there is a possibility of invasion by mosquitoes infected with arboviruses. The output from the BioTEMS model to aid in IMM can be improved in the Chabahar area through the input of additional data. It is recommended that increased monthly surveillance for three or more years be implemented in the area of Chabahar to aid in mitigation and vector control efforts.

Vaux and Medlock (2015) implemented the following surveillance procedures in port areas in the United Kingdom: 1) Establish a baseline of mosquito breeding habitats, 2) Conduct active surveillance for invasive mosquitoes at the ports, 3) Identify appropriate surveillance method suited to port environments, and 4) Develop the capability and capacity of port health officers to conduct invasive mosquito surveillance.⁴⁹ In addition to surveillance, prevention of establishment of invasive species into the port area is critical. Application of pesticides on ships, cargo, and port areas can reduce the risk of invasion by mosquitoes; however, the continuous spraying of pesticides is expensive and may damage the environment. Low cost and environmentally friendly methods using new pesticide technologies can be used to lower the risk of the establishment of invasive species while reducing the local mosquito population. Pesticides with mosquito bait can be delivered using devices, such as the ProVector, hung in structures to reduce the mosquito population without the need for spraying for up to several months.^{20,50}

Conclusion

In summary, local transmission of DNV, CHIKV, and ZIKAV have not been documented in Chabahar. The risk is increased with the recent invasion of *Ae. albopictus*, most likely through ports in southeastern Iran. The BioTEMS model

provides high-resolution information that medical and public health officials can use to assess the risk of invasive mosquito species, arboviruses, and integrated mosquito management planning. Active mosquito control and epidemiologic surveillance of mosquitoes and humans, particularly surrounding air and marine ports and in vehicle maintenance facilities are critical in reducing the risk of the introduction and establishment of arboviruses in Chabahar.

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Conflict of Interest: None declared.

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