Socio-Environmental Variability and Barmah Forest Virus Disease Transmission: A Review of Epidemiological Evidence and Future Prospects

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Abstract
Barmah Forest Virus (BFV) disease is the most rapidly emerging mosquito-borne disease in Australia. BFV transmission depends on factors such as climate, virus, vector and the human population. However, the impact of climatic and social factors on BFV remains to be determined. This paper provides an overview of current research and discusses future research directions on the BFV transmission. These research findings could be regarded as an impetus towards BFV prevention and control strategies.

1. Introduction
Arboviruses are an increasing threat to population health globally (Liu et al., 2008). Arboviruses are viruses that are “maintained in nature by a biological transmission cycle between susceptible vertebrate hosts and haematophagous arthropods” (World Health Organization Scientific Group, 1967). Climate change is expected to increase the activity of climate-sensitive arboviruses and their vectors by gradually raising the temperature and sea levels, and the changing rainfall patterns globally (Russell, 2009). Australia is not immune to these climatic changes and therefore, a mosquito-borne disease has become a significant concern for Australians (Russell, 2009 and Jacups et al., 2008). The Department of Health and Aging report states that “the climate warms up, the tropical weather zone in Australia will spread south, bringing with it disease vectors found prevalent in tropical weather zones” (Department of Health and Aging, 2007).

1.1 Characteristics and Ecology of Barmah Forest Virus Disease
In Australia more than 75 arboviruses have been documented, but only 12 are related to human disease and all are transmitted by mosquitoes (Russell, 1995 and Mackenzie et al., 1994) of the arboviruses important in human infection, Barmah Forest virus (BFV) (Alphavirus, Togaviridae) is the second commonest mosquito-borne disease (after Ross River virus), causing BFV disease (Russell and Kay, 2004) which is unique to Australia (Russell and Kay, 2004 and Mackenzie et al., 1998). BFV was named after it was first isolated from Culex annulirostris mosquitoes trapped in the Barmah Forest of the Murray River in northern Victoria, Australia in 1974, but it was only shown to be pathogenic to humans since 1988 (Merianos et al., 1992). BFV has been isolated from over 73 species of mosquitoes belonging to Aedes and Culex genera. The symptoms of the disease may include arthralgia, myalgia, fever, rash and polyarthritis. Other uncommon symptoms are glomerulonephritis and Guillain-Barre syndrome which includes kidney inflammation. Sometimes the symptoms may persist for up to several months. The disease is usually non-fatal and affects people of any age and gender. The incubation period of the disease is about 7-9 days. Since 1988, BFV disease has been reported in every state and territory in Australia (Queensland Department of Health, 2009). Over the last fourteen years (ie, 1995-2008), a total of 15, 592 laboratory confirmed BFV cases (1,114 cases/year) have been reported in Australia with over 50% of the cases (n=8,050) from Queensland (Queensland Department of Health, 2009). BFV is a seasonal disease with peak occurrence in February (summer) and March (autumn) (Kelly-Hope et al., 2002). There was an increasing trend of BFV transmission in Australia over recent years (Queensland Department of Health, 2009). The reasons for this increased BFV may include urban developments in or near wetland and salt-marsh habitats, and socio-ecologic changes (Tong, 2004 and Russell, 2002). The major risk factors for BFV disease transmission include behavioural, environmental and ecological and climatic changes (e.g., temperature and rainfall), people's movement, and vector control programs. BFV is an emerging disease and there has been an increasing interest on the determination of major
risk factors for the disease transmission. Therefore, to identify current knowledge gaps and future research needs, this paper critically reviewed the impact of climatic, social and environmental variability on the transmission of BFV disease and provided an overview of research development and future research directions in this emerging field. The ecology of BFV is complex. For the transmission of BFV, the virus and its reservoir hosts (Russell, 1995), vector and the human population and climatic (Reves et al., 1994) conditions are key factors (Mackenzie et al., 1998). Marsupials such as kangaroos, wallabies are the possible reservoir hosts for BFV disease. The distribution and abundance of the reservoir population will affect the availability of virucidal individuals to mosquitoes and a non-immune reservoir population leads to increased virus activity (Boughton et al., 1984). Weather conditions such as temperature and rainfall directly affect mosquitoes breeding, survival, and abundance and the extrinsic incubation period and adult longevity (Russell, 1998, Russell and Dwyer, 2000). Humidity and tides are additional important considerations that can also influence the transmission of the disease (Naish et al., 2009 and Naish et al., 2006). However, other socio-ecological factors such as human behaviour, lifestyle and immunity also are involved as determinants in the transmission of BFV disease. In this study, we reviewed the previous studies conducted in determining the risk factors for the transmission of BFV disease and mapped the spatial distribution of BFV disease in Queensland, Australia in order to identify the high-risk areas for the transmission.

2 Literature Review

2.1 Literature Search Strategies

In addition to our research, systematic literature search was conducted to identify all relevant studies on the climatic, social and environmental factors and BFV disease. A series of electronic databases such as MEDLINE (via EBSCOhost), ScienceDirect, Web of Science and Pub Med were searched. Literature searches were conducted in May 2009, with no date or language restriction. The databases were searched with the following key words or MeSH terms: "Barmah Forest Virus" AND "climate" OR "social" OR "environmental" OR "climatic" OR "rainfall" OR "temperature" OR "ecological" OR "humidity." We have assessed all the publications obtained through the literature search based on the titles and abstracts and selected only those suitable for inclusion. Full copies of all relevant papers were then obtained, and critically reviewed. All studies were conducted in Australia; 6 papers were published during 2000 to 2009 (Table 1).

<table>
<thead>
<tr>
<th>Study details</th>
<th>Study design</th>
<th>Major findings</th>
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</thead>
<tbody>
<tr>
<td>Doggett et al., 1999, Australia</td>
<td>An epidemiological study investigation</td>
<td>Found a relationship between rainfall and high tide.</td>
<td>Stated that climatic factors may be involved in the mosquito distribution however statistical analysis was not conducted.</td>
</tr>
<tr>
<td>Bit et al., 2000, Queensland, Australia</td>
<td>Correlation analysis</td>
<td>Southern oscillation index was associated with BFV transmission</td>
<td>Stated that there was a variation in the spatial and temporal distribution of BFV disease but spatiotemporal analysis was not conducted.</td>
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<tr>
<td>Passmore et al., 2002, Victoria, Australia</td>
<td>An epidemiological study investigation</td>
<td>Stated that there was a relationship between rainfall and mosquito density</td>
<td>Assessed the relationship between mosquito distribution and rainfall however modelling analysis was not conducted.</td>
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<tr>
<td>Teng et al., 2005, Queensland, Australia</td>
<td>BFV disease mapping for the period 1993-2001</td>
<td>An increase in the geographic distribution of BFV cases in Queensland over recent years</td>
<td>Mapped the distribution of BFV disease in Queensland however risk factor analysis was not conducted.</td>
</tr>
<tr>
<td>Naish et al., 2006, Queensland, Australia</td>
<td>Ecological time series analysis</td>
<td>Identified minimum temperature and high tide as key determinants for BFV transmission</td>
<td>Time series models were analysed and the key determinants involved in the transmission of BFV disease in Gladstone region in Queensland were determined.</td>
</tr>
<tr>
<td>Naish et al., 2009, Queensland, Australia</td>
<td>Ecological time series analysis</td>
<td>Identified minimum temperature, social factors and high tide as key predictors for BFV transmission</td>
<td>Regression models were analysed and the potential risk factors involved in the BFV disease transmission in Coastal Queensland region were determined.</td>
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</table>
2.2 Key Predictors of BFV Transmission

The primary objectives of our own research were to assess the impact of climate variability, social and environmental factors on the transmission of BFV disease, and the importance of developing forecasting systems for the control and prevention of this emerging vector-borne disease in Australia. We collected data for the period 1992 to 2001 from relevant government agencies on climate variables, social and environmental variables and notified cases of BFV disease for six coastal cities in Queensland, Australia. The computerised data set of notified BFV cases, climate and tidal data were obtained from Queensland Health, Australian Bureau of Meteorology and Queensland Transport, respectively. Population and socioeconomic status data (SEIFA index) were supplied by Australian Bureau of Statistics. Time-series regression models were performed to assess the impact of climate variability on BFV transmission in coastal Queensland cities (Naish et al., 2009). We run several models and obtained the best-fit model for the BFV dataset with different sets of predictor variables. The models included the number of BFV cases as the response variable and the climate and tidal variables in the current month and with a moving average of lags 1-2 months, and SEIFA index, as explanatory variables. The best-fit model was selected based on the deviance reduction as measured with Chi-squared test statistic and the Akaike's Information Criterion (AIC) value. The model with smallest AIC value and deviance showed that BFV counts were positively and statistically significantly associated with maximum temperature (β = 0.139, p = 0.000) and high tide (β = 0.005, p = 0.000) and negatively and statistically significantly associated with SEIFA index (β = -0.010, p = 0.000). The models were adjusted for confounding effects of seasonality and population size. The goodness-of-fit test indicates that the model developed was the most parsimonious for this dataset with AIC = 3532.97, Pearson \( \chi^2 \) value of 1.05, deviance value = 0.95 and Omnibus likelihood ratio of 444.3 (Naish et al., 2009). We found that temperature, high tide and socio-economic conditions were key risk factors in the transmission of BFV disease in coastal Queensland. In another study, we performed an ecologic time-series analysis to examine the association between climate variability and the transmission of BFV disease for the years 1992 to 2001 in Gladstone region, Queensland, Australia. The autorregressive integrated model was used to examine the relation between the climate variability, tides, and the monthly incidence of notified BFV infections. As maximum and minimum temperature were highly correlated with each other (\( r = 0.95 \)), two separate models were developed. The correlation coefficients were in the range of 0.037 to 0.385 for actual maximum and minimum temperatures, 0.020 to 0.129 for rainfall and 0.022 to 0.152 for relative humidity (Naish et al., 2006). Monthly minimum temperature and high tide at the current month played a significant role in the transmission of BFV disease in Gladstone with a log-likelihood of \(-79.33\) and \(\text{AIC} = 168.66\). We found that temperature and high tide were the key predictors in the transmission of BFV disease in Gladstone. In a previous study, Tong et al. (Tong et al., 2005) used GIS mapping tools to visualise the outbreaks of BFV in Queensland, Australia. For that study, they used the computerised data set on the notified BFV cases in Queensland for the period of 1993 to 2001. They found that there has been an increase in the geographic distribution of the notified BFV cases in Queensland over the last decade. Passmore et al. (Passmore et al., 2002) obtained the climate data for the years 2001 and 2002 from Victoria, Australia, and compared the relationships between rainfall from each mosquito trapping site and mosquito counts. They found that mosquito counts were increased when rainfall was increased. Bi and his associates (Bi et al., 2000) used BFV cases from 1992 to 1996 in Queensland, Australia, and found that there was an association between positive southern oscillation index (SOI) values and sea level, which had an impact on the breeding sites of some Aedes mosquitoes. The reported place of onset for each case was used to characterise the geographic distribution of the BFV infection within Queensland. Doggett et al. (Doggett et al., 1999) obtained data on climate, BFV and mosquitoes in New South Wales, Australia from 1994 to 1995 and studied the relationships between climate and mosquitoes. They found that mosquito populations had increased due to the increased levels of rainfall and high tides which then caused increased BFV cases.

2.3 Other Risk Factors

Many other risk factors such as virus, vector, host, and environment are involved in the BFV transmission cycles. Changes in weather, virus strain, mosquito populations, survival, and breeding; human activities, movement and immunity, and socioeconomic status may all contribute to the transmission cycles of BFV disease. Changes in farming practices-such as building dams and irrigation canals, and identification of new wetlands and vegetation - have created ideal breeding habitats for saltmarsh and freshwater mosquito species. Deforestation due to cultivation and urban
development due to increase in human movements could increase the potential for BFV transmission (Mackenzie et al., 2000, Russell, 2009, Lindsay and Mackenzie, 1998). Tourism and travel have also become important mechanisms for facilitating the BFV and its vectors. Climatic changes periodically may also influence the local weather conditions and the life cycle of the disease reservoirs and cyclic changes in human outdoor activities. However, few data were available on many of these factors (eg: human movements and immunity), and therefore, it might be difficult to explain a broad spectrum of reasons for the increase in the transmission of BFV disease.

2.4 Forecasting

The development of disease outbreak forecasting systems is important in the control and prevention of mosquito-borne diseases. A large-scale public health intervention is usually required during an outbreak. Early warning systems based on weather forecasts can assist in improving vector control in high-risk areas. Therefore, analysis based on GIS may have an opportunity to develop an early warning system to predict the outbreaks in high-risk zones and improve vector control and public health intervention.

2.5 Mapping the BFV outbreaks

We mapped the distribution of BFV cases using Geographic Information Systems (GIS) to identify high-risk areas and predict outbreaks of BFV in Queensland, Australia (Figure 1). It shows that the disease is largely concentrated near the coast and is found in both tropical and subtropical Queensland, Australia, where the salt marsh mosquito, Aedes vigilax, and the fresh water species, Culex annulirostris, are vectors of BFV disease.

Figure 1: GIS-based distribution of notified BFV cases in Queensland, Australia, 1992-2001 (Numbers in parentheses indicate the number of localities)
Mapping the high-risk areas or hot spots may facilitate an assessment of the breeding habitats of the mosquito species of BFV disease. Using the mapped distribution of BFV in Figure 1, we identified several hotspots for BFV disease which were found along the coastal and inland areas (Naish et al., 2011).

2.6 Future Prospects
Our future research aims at applying GIS tools for assessment of BFV disease outbreaks in Queensland. The main focus will be on determining the correlation of key climatic, tidal and socio-environmental factors associated with BFV disease. This relationship will be used in conjunction with GIS to map BFV distribution vector breeding sites. The aim is to show how GIS combined with the predictors of BFV disease may help to control and prevent BFV transmission and to reduce the disease burden. As such information when mapped together creates a powerful tool to analyse distribution of micro-organisms and their relationship to different ecological niches, and may dramatically improve our ability to quantify the impacts of climatic and ecological changes on BFV and other mosquito-borne diseases. The ability to predict outbreaks of BFV disease will greatly enhance the efficacy of prevention efforts and will substantially reduce costs of prevention with efficient targeting of high-risk areas.

3 Conclusions
We found that socio-environmental variables such as temperature, SEIFA index and tides have played a key role in the transmission of BFV disease in Queensland. In this study, baseline mapping of the BFV data indicated that there are hot spots or high-risk areas for the transmission of BFV disease. These research findings may be useful for planning BFV disease control and risk management programs.

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