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Short Communication

Transmission potential of Zika virus infection in the South Pacific

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SUMMARY

Objectives: Zika virus has spread internationally through countries in the South Pacific and Americas. The present study aimed to estimate the basic reproduction number, R_0, of Zika virus infection as a measurement of the transmission potential, reanalyzing past epidemic data from the South Pacific.
Methods: Incidence data from two epidemics, one on Yap Island, Federal State of Micronesia in 2007 and the other in French Polynesia in 2013–2014, were reanalyzed. R_0 of Zika virus infection was estimated from the early exponential growth rate of these two epidemics.
Results: The maximum likelihood estimate (MLE) of R_0 for the Yap Island epidemic was in the order of 4.3–5.8 with broad uncertainty bounds due to the small sample size of confirmed and probable cases. The MLE of R_0 for French Polynesia based on syndromic data ranged from 1.8 to 2.0 with narrow uncertainty bounds.
Conclusions: The transmissibility of Zika virus infection appears to be comparable to those of dengue and chikungunya viruses. Considering that *Aedes* species are a shared vector, this finding indicates that Zika virus replication within the vector is perhaps comparable to dengue and chikungunya.

1. Introduction

Zika virus is a mosquito-borne *Flavivirus* transmissible from human to human through bites of *Aedes* species mosquitoes. Zika virus not only shares a common vector species with dengue virus and chikungunya virus,[1] but the clinical signs and symptoms of Zika virus infection are also partly the same as those of dengue fever and chikungunya virus infection.[2] In recent years, the virus has spread internationally through countries in the South Pacific and Americas.[3,4] Due to growing concerns over the association between Zika virus infection in pregnant women and microcephaly in the fetus,[5] the risk assessment and management of infection has attracted global attention.

While the virus has spread geographically following the path of chikungunya virus along with the abundance of *Aedes spp*,[6–8] the transmissibility of the virus has yet to be quantified statistically. This estimation is of the utmost importance, because the efforts required to control Zika virus infection will depend on the transmission potential. The present study aimed to estimate the basic reproduction number (R_0) of Zika virus infection – the average number of secondary human cases generated by a single primary human case – through an analysis of past epidemic data from the South Pacific.

2. Materials and methods

Time-dependent incidence data were retrieved from two published studies.[2,9] One occurred on Yap Island, Federal State of Micronesia in 2007,[9] while the other occurred in French Polynesia in 2013–2014.[2] Case data of the earlier epidemic were collected based on laboratory diagnosis (either by detecting Zika virus RNA or antibody; $n = 108$), while the later epidemic data were derived from syndromic surveillance of suspected cases ($n = 8581$). The number of new cases in every week could be yielded from both studies.

R_0 was estimated from the early exponential growth rate. First, the exponential growth rate was estimated from the weekly data using the Poisson distributed likelihood function, as proposed by Nishiura et al.[10] Subsequently, the estimated growth rate 'r' was converted into R_0 using the following renewal equations that

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describe the incidence in humans $j_h(t)$ and vectors $j_v(t)$:

$$j_h(t) = R_{hv}\int_0^\infty g_{hv}(\tau)j_v(t-\tau)d\tau \quad (1)$$

$$j_v(t) = R_{vh}\int_0^\infty g_{vh}(\tau)j_h(t-\tau)d\tau \quad (2)$$

where R_{hv} and R_{vh} are the average number of human cases generated by a single infected vector and vector infections generated by a single human case, respectively. $g_{hv}(\tau)$ and $g_{vh}(\tau)$ are density functions of the time from vector infection to human infection and from human infection to vector infection, respectively. Assuming that the incidence of both humans $j_h(t)$ and vectors $j_v(t)$ grow exponentially with the rate r in a fully susceptible population, we obtain

$$R_0 = \sqrt{R_{hv}R_{vh}} = \sqrt{\frac{1}{M_{vh}(-r)M_{hv}(-r)}} \quad (3)$$

where $M_{vh}(-r)$ and $M_{hv}(-r)$ are the moment-generating functions of human to vector and vector to human transmissions, respectively, given growth rate r.[11,12] Table 1 shows published estimates that parameterized $M_{vh}(-r)$ and $M_{hv}(-r)$. Assuming that each distribution is exponential with the mean values in Table 1, equation 3 agrees with Pinho et al.[13] The impact of parameter uncertainty on R_0 was examined using Latin hypercube sampling (LHS) with uniformly distributed parameters (Table 1).[14,15]

3. Results

Figures 1A and 1B compare the observed and predicted early growth of cases, assuming that the exponential growth has continued for the first 3–5 weeks. From Yap Island data, the maximum likelihood estimate (MLE) of R_0 was 4.5 and 5.8 for the assumed 4-week and 5-week exponential growth period. Due to the scarcity of data, only an upper bound ($R_0 \leq 2.7$) was obtained for the 3-week exponential window. Analyzing the data from French Polynesia, R_0 was estimated at 1.8, 2.0, and 2.0 for 3-week, 4-week, and 5-week exponential growth, respectively (Figure 1C). The uncertainty analysis indicated that MLE of R_0 for Yap Island could range from 2.8 to 12.5 depending on the length of generation time.[15] Similarly, R_0 for French Polynesia could range from 1.5 to 3.1.

4. Discussion

R_0 of Zika virus infection was estimated analyzing datasets from the South Pacific. MLE of R_0 for the Yap Island epidemic was in the order of 4.3–5.8 with broad uncertainty bounds due to the small

Table 1
Parameters used in the model of Zika virus transmission

Parameter	Biological meaning	Value (per day)	Reference	Assumed range
μ_h	Human mortality rate	$1/(365\times60)$	Assumed	N/A
ε_h	Rate of acquiring infectiousness	1/5	15, 19	1/12–1/3
γ_h	Recovery rate	1/11	15, 20	1/17–1/6
μ_m	Mosquito mortality rate	1/14	15, 21	1/23–1/10
ε_m	Extrinsic incubation rate	1/10	15, 19	1/23–1/6

N/A, not applicable.

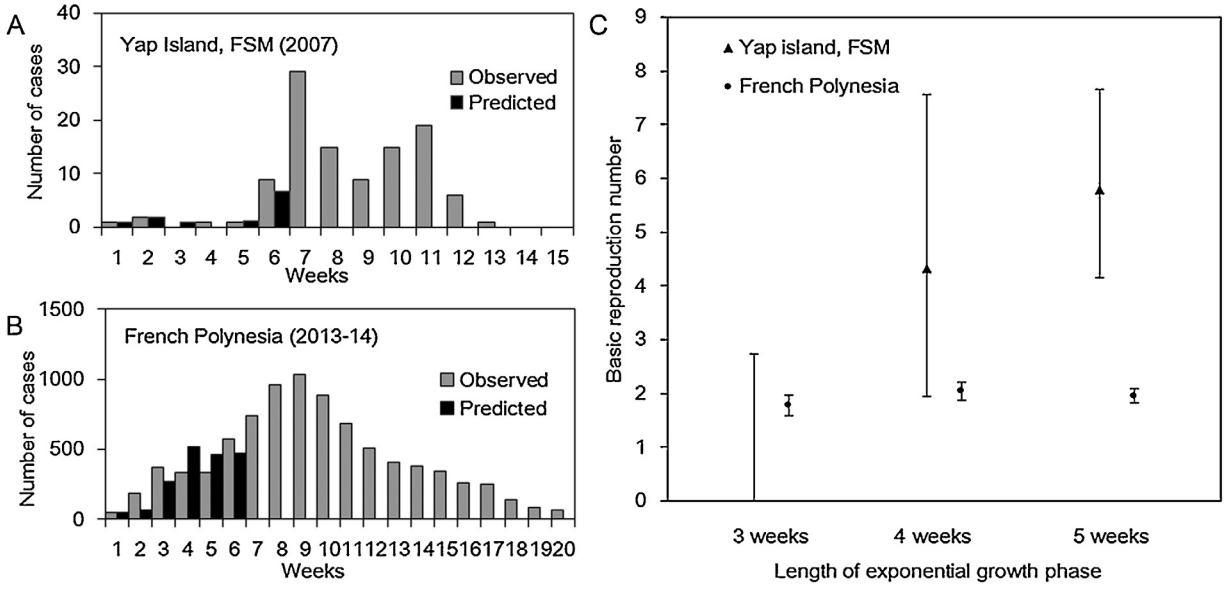

Figure 1. Transmission dynamics of Zika virus infection on Yap Island, 2007 and French Polynesia, 2013–2014. (A) (B) Comparison of observed and predicted weekly numbers of new cases during the early period of the Zika virus epidemic. Predictions are shown when an exponential growth was assumed to continue for the first 4 weeks. (C) Estimates of the basic reproduction number. Dots represent the maximum likelihood estimates, while whiskers extend from the lower to upper 95% confidence intervals as derived from profile likelihood. For Yap Island, the maximum likelihood estimate was not calculable using only the first 3 weeks due to the scarcity of cases. Case data for the Yap Island epidemic were collected based on laboratory diagnosis (either by detection of Zika virus RNA or antibody; $n = 108$), while data for French Polynesia were derived from the syndromic surveillance of suspected cases ($n = 8581$).

sample size. The MLE of R_0 for French Polynesia ranged from 1.8 to 2.0 with narrow uncertainty bounds. Both values are broadly consistent with empirical estimates of R_0 for dengue and chikungunya virus infections.[16,17] Considering that *Aedes spp* are a shared vector, this finding indicates that Zika virus replication within the vector is perhaps comparable to that of dengue and chikungunya viruses.

Caution must be exercised in the interpretation of these estimates. First, the R_0 of a vector-borne disease is not universally applicable to any other setting in the world. In particular, the abundance of *Aedes spp* is not substantial in temperate countries and thus these estimates will only help to understand the transmission potential in geographic areas where Zika virus transmission could be sustained. In addition, it should be noted that the implications for control could also depend on the fraction of sexual transmission among all secondary transmissions.[18] Second, both datasets involved an issue of under-ascertainment, and syndromic data are non-specific. To overcome these issues, sero-epidemiological surveys should ideally be implemented to capture the overall transmission dynamics. Third, the present approach might not have sufficiently captured demographic stochasticity due to the absence of finer time-scale data than weekly counts of cases.[19,20,21]

In conclusion, the transmission potential of Zika virus infection in the South Pacific was quantified, demonstrating that the transmissibility of this emerging virus is comparable to those of dengue and chikungunya viruses. Vector control programs should be planned with reference to these estimates.

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