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Predicting Ross River Virus Infection by Analysis of Seroprevalence Data

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Abstract Infection with *ar*thropod-*bo*rne (arbo)viruses presents a significant and growing public health threat to the resident population of Queensland (QLD), the north-eastern state of Australia. Clinical infection with Ross River virus (RRV) is the most commonly detected, and arguably most debilitating, of Australia's 75 known indigenous arbovirus species. Development of prediction models to forecast arbovirus epidemics aims to provide accurate and reliable tools that may facilitate planned interventions by local and state authorities to curb disease transmission. Acute immunoglobulin (Ig)M-positive enzyme-linked immunosorbent assay results are often misleading, with interpretation cautioned. As such, this serological testing was recently excluded as a means to confirm cases of arbovirus infection in Australia. The purpose of this study was to investigate the seroepidemiological value of acute IgM-positive results across QLD by correlating with RRV case reports and to develop a mathematical model to predict RRV outbreaks. Blood samples from patients throughout QLD suspected of arboviral infection were tested for RRV, with numbers for various serology results grouped by geographical region. The serology data were compared with case reports for each respective region by multiple regression in order to determine any relationships. RRV IgM-positive results correlated significantly to the number of case reports per region ($P < 0.05$). An estimated multiple regression equation was used to predict RRV case reports from a subset of data extracted for the period December 2015 and January 2016. Predicted cases based on IgM-positive/IgG-negative serology showed no significant correlation to the respective case reports for each region ($P > 0.05$). Hence, these findings failed to validate the potential use of IgM-positive seroprevalence to predict RRV infection with sufficient accuracy for diagnostic purposes. A possible indirect value may exist, however, in analysing pooled seroprevalence data, which may better inform concurrent surveillance measures and thereby enhance the accuracy of RRV outbreak forecasts.

Keywords: *vector-borne disease, arbovirus, Ross River virus, Australia, seroprevalence, outbreak, infectious disease modelling*

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1. Introduction

Vector-borne infectious diseases, principally those transmitted by arthropod insects such as mosquitoes and ticks, are a growing public health threat. Many are emerging or re-emerging diseases, but their patterns of distribution are extremely volatile due to the high variability among pathogens, hosts, vectors, regional environments and landscapes [1,2,3]. The geographical range of causative agents is restricted to the areas inhabited by their vectors and, if zoonotic, their reservoir hosts, so the escalating impact of climate change and dramatic weather events on habitat suitability is of major concern [4]. Shifts in societal, demographic and epidemiological characteristics of human populations, including urbanisation, international travel and migrant integration, also influence how environmental risk affects the frequency of disease cases, patient outcomes and ultimately the burden of these vector-borne diseases. Mathematical modelling is a technology that is pivotal to integrating infectious disease data retrieval and analysis with vector-borne disease research in order to enhance prevention and control measures and to inform public health management policy.

The development of surveillance-based prediction models for *ar*thropod-*bo*rne (arbo)virus epidemics offers a potentially invaluable tool to help combat the far-reaching emerging health impact that is caused globally by mosquito transmission of flaviviruses (notably dengue, yellow fever, Japanese encephalitis, West Nile and Zika) and alphaviruses (notably chikungunya and Ross River virus, RRV) [5]. These statistical models could be utilised

to predict outbreak risk and thereby to reduce epidemics by such early interventional actions as drainage of still water, spraying residual insecticides and/or warning communities via news channels, mobile device apps and social media networks [6,7,8].

The mosquito-transmitted viral disease Ross River fever is the cause of profound public health problems in Australia, especially Queensland (QLD), the Northern Territory and the Kimberley region of Western Australia [9,10,11]. For almost a decade after the identification of RRV [12], very few patients were identified as having a clinical infection with this pathogenic agent because diagnostic screening was restricted to a research setting using an in-house developed test method. Following the 1985 commercial release of an enzyme-linked immunosorbent assay (ELISA) to detect anti-RRV immunoglobulin (Ig)M antibody, epidemic polyarthritis (EPA; clinical RRV infection) became a nationally notifiable disease in 1990 [13]. Nationwide annual RRV diagnoses rose from 20-50 pre-commercial testing to a current figure of several thousand [14].

The Australian National Notifiable Diseases Surveillance Scheme received notification of 47,256 cases of vector-borne diseases for the recent period from January 2013 to December 2017 [14]. RRV accounted for 29,843 (63.1%) of these. While the average number of notifications of RRV infections over this five-year duration is around 4,500 per annum, 9,554 cases were reported in 2015 [14]. RRV has been isolated from at least 40 different mosquito species [15]. In addition to its detection in mosquitoes and humans, serological surveys have found widespread infection with RRV among kangaroos, wallabies, bandicoots and other Australian marsupials [16,17]. The virus has also been recovered from horses, cattle, goats, sheep, dogs and birds [18,19]. Therefore, it is likely that RRV is being maintained in zoonotic cycles involving native animals and birds which are putative natural reservoir hosts [20].

Prompt and accurate notification of laboratory-confirmed and probable cases is an important component of arbovirus surveillance as this information enables public health units to initiate a timely and commensurate response to an outbreak [21]. Serology-dependent case definitions for RRV infection have been plagued with incidences of false-positive reports [22,23,24]. This has arisen via a combination of reliance solely on IgM results, the persistence of IgM in peripheral blood, antibodies cross-reactive to other alphaviruses such as Barmah Forest virus (BFV), issues relating to original antigenic sin, suboptimal ELISA kits, and irregular inter-laboratory methodologies and diagnostic criteria [22]. The inconsistent notification criteria for arbovirus infection by serological determinants recently received criticism within the medical laboratory science profession in Australia [24]. On the recommendation of the National Arbovirus and Malaria Advisory Committee, the Case Definitions Working Group (CDWG) of the Communicable Diseases Network Australia undertook a review of surveillance case definitions for RRV infections that was implemented at the start of January 2016 [24]. Queensland Health stated that the "historical data prior to the change of case definition will continue to be considered unreliable" [23].

In order to ensure the collection of reliable and consistent data the CDWG revised the criteria for the categorisation of confirmed or probable RRV infection notifications [24]. Infection of RRV is confirmed if any one or more of the following is identified in blood, plasma or serum obtained from the patient: isolation of virus; detection of viral nucleic acid; or IgG seroconversion, as determined by a four-fold or greater rise in anti-RRV IgG antibody. Except for specimens in which IgG is detected $\geq$ 3 months prior, the presence of both IgM and IgG antibodies is even more suggestive of a probable RRV infection [24].

An average incubation period for RRV, i.e. the time from being bitten to presenting clinical symptoms, is around one week. While patients often seek medical services as soon as they are ill, whereupon their blood is tested, the delay in receiving and handling the sample may mean that it is too late for the virus to be isolated or its RNA to be detected [22-24]. Furthermore, virus isolation is a time-consuming procedure. Hence, there is the need for a more convenient technique, that of detection of anti-RRV antibodies (Table 1).

Table 1. Potential indications of test results for arboviruses, including RRV, from commonly occurring IgM and IgG serology permutations

IgM	IgG	Key	Definition
Negative	Negative	NN	No evidence of acute or past infection * Acute sample of clinical illness prior to antibody development *
Negative	Equivalent	NE	Distant past infection indicated
Negative	Positive	NP	Past infection indicated
Equivalent	Negative	EN	Possible early infection * False equivalent non-specific IgM * Cross reaction to another infection, e.g. CMV, EBV, Parvovirus *
Equivalent	Equivalent	EE	Possible early infection * Distant past infection with false equivalent or cross-reactive IgM
Equivalent	Positive	EP	Possible late infection indicated * Possible past infection with false equivalent or cross-reactive IgM
Positive	Negative	PN	Possible early infection * False positive non-specific IgM * Cross reaction to another infection, e.g. CMV, EBV, Parvovirus *
Positive	Equivalent	PE	Possible mid-stage seroconversion Possible distant past infection with false positive or cross-reactive IgM
Positive	Positive	PP	Possible acute infection indicated * Possible past infection with false positive or cross-reactive IgM

* Guideline: repeat convalescent testing to identify seroconversion or a four-fold or more increase in IgG titre. CMV, cytomegalovirus; EBV, Epstein-Barr virus. Adapted from Sullivan Nicolaides Pathology Arbovirus Reports 2015.

A combination of serology results that is either IgM-positive and IgG-negative (PN) or positive for both IgM and IgG (PP) has various interpretations, for which the IgM result is key (Table 1). This study proposes that either PN or PP serology from a given locality may be predictive of seroconversions or notifications in the local community in which that patient resides. If by linear regression a significant relationship exists between rates of PN results and infection notifications throughout QLD, a predictive mathematical model for surveillance and subsequent interventional response to RRV outbreaks could be applied across the state.

2. Materials and Methods

2.1. Laboratory Serology Testing

From QLD residents suspected of RRV infection by medical examination, 716 anonymised patient sera received in local authority pathology laboratories during the months of December 2015 and January 2016 were tested by commercially available anti-RRV IgM and IgG ELISA (PanBio Ltd., Sinnamon Park, QLD, Australia) (Table 2). Serology data were collated prospectively together with the date of test, age, gender, residential location and postcode. Patients excluded from this study included interstate travellers, those with a previously positive IgG result recorded ≥ 3 months earlier due to confounding implications of prior infection, and those in whose sera IgM to viruses of similar antigenic affinity (e.g. cytomegalovirus or BFV) was detected.

2.2. Population Statistics and Groupings

The quantitative values of each serology permutation for RRV were grouped together by QLD region, testing date ranges (1-11, 12-31 December 2015 and 1-15, 16-31 January 2016), gender and age ranges (0-24, 25-49, 50-74, and ≥ 75 years). Projected population data by QLD region, age range and gender were extracted from the Australian Bureau of Statistics 2015 database [25].

2.3. Infection Notification Data

Notification data for confirmed or probable cases of infection with RRV for onset dates between 1 December 2015 and 31 January 2016 were extracted and supplied by the Notifiable Conditions System, Public Health Unit, Queensland Health. The samples were collected from 19 regions throughout QLD (examined at statistical area level 4 based on the 2011 Australian Statistical Geography Standard) but principally from Brisbane, Bundaberg, Cairns, Gold Coast, Mackay, Rockhampton, Toowoomba and Townsville (Figure 1).

2.4. Predictive Model Development and Analysis

For prospective IgM and IgG serology results, tests for RRV infection were collated with respective epidemiological data (Table 2). In order to derive equations linear regression model analysis was performed between notification reports and the corresponding rates of IgM & IgG permutations (Table 3). IgM-positive/IgG-negative (PN) and IgM-positive/IgG-positive (PP) serology results from each location were shown by regression analysis to be significantly correlated ($P < 0.05$), but the correlation value obtained for PP ($R^2 = 0.23$) was lower than for PN ($R^2 = 0.53$) (Table 3). Therefore, the mathematical equation for PN was subsequently used to predict the number of notification reports during a specified period for each region of QLD.

Serology data and notification rates were normalised between QLD regions by calculating their ratio per 100,000 residents (Table 4), according to the projected 2016 population size [25]. The normalised data set was also analysed by multiple regression to determine any statistically significant association between serology results and cases of infection which might indicate a relationship common among QLD regions.

Table 2. RRV serology results and case notifications for December 2015 and January 2016 by QLD region

Region	RRV serology results for December 2015 and January 2016										Notified cases *		
	NN	NE	NP	EN	EE	EP	PN	PE	PP	Total sera	Confirmed	Probable	Total cases
Brisbane East	14	1	19	0	0	1	1	0	1	37	14	3	17
Brisbane North	7	0	10	1	0	0	2	0	4	24	26	3	29
Brisbane South	10	0	10	0	0	1	1	0	4	26	15	8	23
Brisbane West	7	1	14	0	0	2	1	0	4	29	13	2	15
Brisbane Inner City	8	0	5	0	0	0	0	0	4	17	5	5	10
Cairns	33	2	28	0	0	2	3	1	4	73	21	26	47
Darling Downs – Maranoa	0	1	6	0	1	0	1	0	0	9	18	9	27
Fitzroy	6	2	38	0	0	5	2	0	8	61	25	5	30
Gold Coast	14	0	15	0	0	4	1	0	6	40	24	5	29
Ipswich	13	2	18	0	0	2	1	1	3	40	10	8	18
Logan – Beaudesert	6	0	9	0	0	2	1	0	3	21	9	1	10
Mackay	8	0	12	0	0	1	0	0	3	24	7	4	11
Moreton Bay North	12	1	17	0	0	2	0	0	5	37	12	8	20
Moreton Bay South	10	0	20	1	0	1	1	0	6	39	15	6	21
Queensland Outback	4	0	6	0	0	0	1	0	0	11	6	4	10
Sunshine Coast	38	1	59	1	0	8	2	0	6	115	23	6	29
Toowoomba	3	1	5	0	0	2	0	0	1	12	0	1	1
Townsville	18	2	23	1	1	1	1	1	5	53	18	6	24
Wide Bay	14	0	25	1	0	2	0	0	6	48	20	8	28
Total	225	14	339	5	2	36	19	3	73	716	281	118	399

* Notification data supplied by the Notifiable Conditions System, Public Health Unit, Queensland Health.

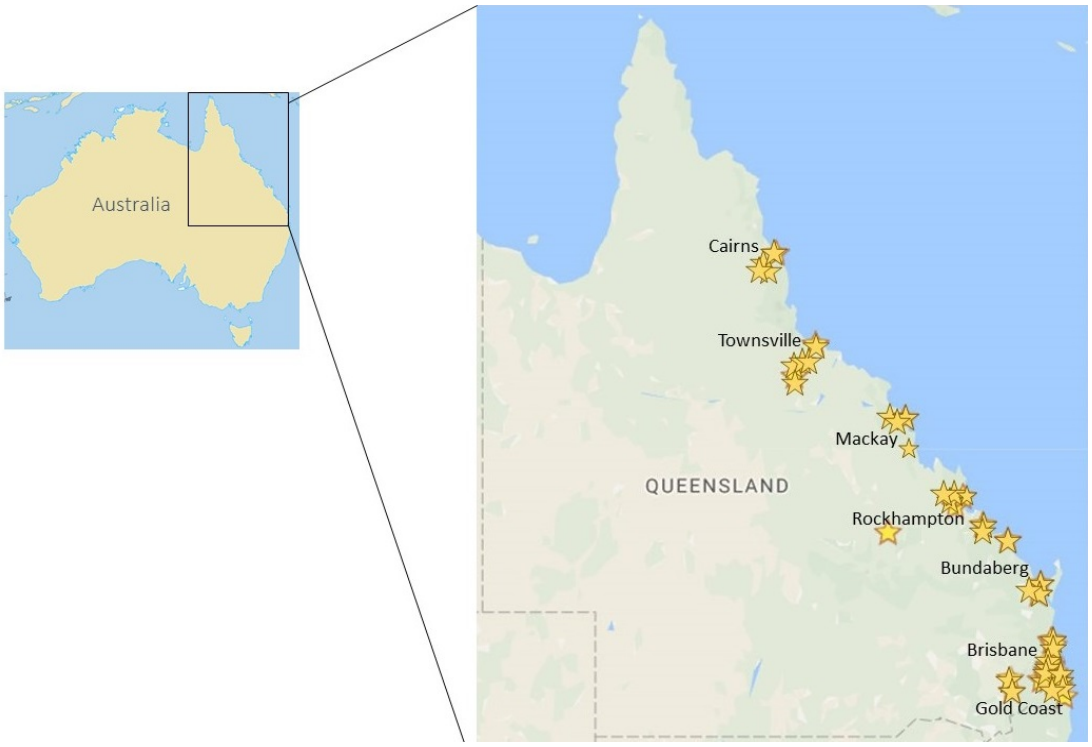

Figure 1. Geographical locations in QLD of blood donors from whom serum samples were obtained

Table 3. Statistical relationship between the sums of serology results and respective case reports of RRV infection by QLD region

		Statistical associations with total notified case reports		
		P value	*R* value	Equations
IgM & IgG permutations	NE	0.1429	0.122	y = 4.54*x + 17.7
	NP	0.0148	0.302	y = 0.434*x + 13.3
	EN	0.2041	0.093	y = 7.06*x + 19.1
	EE	0.5358	0.023	y = 5.03*x + 20.5
	EP	0.1924	0.0978	y = 1.66*x + 17.9
	PN	0.0004/*0.0021	0.53/*0.437	y = 9.33*x + 11.7/*y = 6*x + 8.79
	PE	0.1207	0.136	y = 10.3*x + 19.4
	PP	0.0357	0.234	y = 2.31*x + 12.1

* when regression analysis is performed using only confirmed cases along the x-axis.

Table 4. Predicted cases and reported cases of RRV infection normalised per 100,000 population by QLD region during 16-31 January 2016

Region	PN per 100k population	Predicted cases	*Predicted cases	Reported cases
Brisbane East	0.43	16	11	7
Brisbane North	0.93	20	14	5
Brisbane South	0	12	9	9
Brisbane West	0.53	17	12	5
Brisbane Inner City	0	12	9	2
Cairns	0.4	15	11	29
Darling Downs – Maranoa	0.77	19	13	11
Fitzroy	0.83	19	14	11
Gold Coast	0	12	9	6
Ipswich	0	12	9	6
Logan – Beaudesert	0	12	9	4
Mackay	0	12	9	1
Moreton Bay North	0	12	9	8
Moreton Bay South	0.51	16	12	10
Queensland Outback	0	12	9	3
Sunshine Coast	0.29	14	11	7
Toowoomba	0	12	9	1
Townsville	0.41	16	11	9
Wide Bay	0	12	9	6

* when prediction uses equation obtained from regression analysis performed using only confirmed cases along the x-axis.

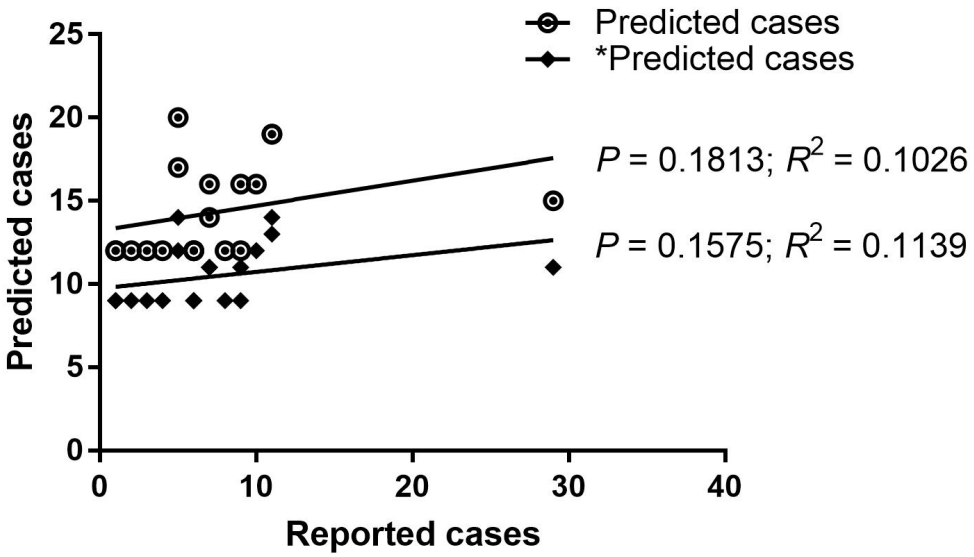

Figure 2. Correlation between reported cases of RRV from 16-31 January 2016 and those predicted cases (target circle – prediction using both confirmed and probable RRV cases; filled diamond – prediction using confirmed RRV cases only)

2.5. RRV Infection Predictions

The total number of PN results and notification rates corresponding to onset dates between 1 December 2015 and 31 January 2016 were normalised for each QLD region per 100,000 population and analysed by linear regression. The linear regression equation (line of best fit) derived from the scatter plot of all data was used to estimate case reports corresponding to serology data for the same two-month period (data not shown). The number of cases of RRV estimated using the dependent variable (that for PN) from serology results and actual notified cases for the period 16-31 January 2016 were compared by regression analysis to identify any relationship (Figure 2).

3. Results

A strongly significant relationship was shown to exist between the total number of RRV serology test requests ordered during December 2015 and January 2016 and the total number of notified cases from each QLD region (P = 0.0014) (Table 2). When the serology data were normalised by ratio per 100,000 population, the correlation between PN and regional cases was still significant ($P < 0.05$). Linear regression model analysis between notification reports and PN serology from each location showed a significant correlation ($P < 0.05$, $R^2 = 0.53$). Hence, the equations obtained from using two different notifications rate, those for RRV confirmed cases ($y = 6*x + 8.79$) and RRV total cases, i.e. including confirmed and probable cases ($y = 9.33*x + 11.7$), were used to predict RRV cases in the SA4 region of QLD during the second half of January 2016 (Table 4). The inherent discrepancy between actual results and predicted results (Figure 2) was minimised by adjustment of PN coefficient and y intercept values in order to reduce the total sum of the normalised error (data not shown). The linear regression between normalised predicted case reports and actual case reports was found to be non-significant ($P > 0.05$) (Figure 2).

4. Discussion

The revision of notification criteria for serology-based RRV infections in Australia that was implemented on 1 January 2016 calls into question the reliability of case records preceding this date [23,24]. The key revision was the implementation of a nationwide collaborative agenda among reporting pathology laboratories to refrain from recognising an acute sample IgM-positive test as a presumptive indicator of infection. A more rigorous laboratory algorithm was to be applied to overcome the occurrence of false positive IgM results [26].

Accordingly, the rationale for this study was to develop a mathematical model predicated on the corrupted data prior to January 2016 and to use this algorithm to predict RRV case reports presently considered valid. A model based on acute IgM-positive serologies should be capable of predicting the rates of currently valid RRV infection notifications based on correlations with case reports that are now known to be unreliable. If the model is accurate this may argue in favour of the presumptive reporting of RRV infection based on IgM-positive results. Yet, a study conducted in Perth, Western Australia, concluded that some 45% of RRV IgM-positive, IgG-negative acute enzyme immune assay results failed to seroconvert whereas around 75% of IgM-positive results tested by either immunoassay or haemagglutination inhibition did seroconvert [22]. In light of this apparent anomaly caution is advised as to the validity of presuming RRV infection from IgM-positive ELISA data. Thus, notifications are reserved until convalescent seroconversion is demonstrated [24].

Patient blood was tested prospectively at the headquarters of Queensland Medical Laboratory Pathology (QML Pathology) in Murarrie, south-eastern Brisbane, where all arbovirus serologies received by QML Pathology collection centres throughout the state are processed. Almost all samples would have come from ambulatory outpatients since QML Pathology performs testing primarily on samples from the community and a smaller subset from private hospitals. Samples from the larger public tertiary care public hospitals are not screened by

this laboratory. A more comprehensive analysis of data would be achieved by collating results from all QLD commercial medical testing laboratories (i.e. including Sullivan Nicolaides Pathology, Pathology Queensland, Mater Pathology and Medlab Pathology). However, there is no reason to consider that the sample set examined was not representative and, moreover, the restriction served as a convenient method of semi-random statistical sampling.

The linear regression model developed herein using both PN and PP anti-RRV antibody results was able to predict correctly when case numbers were low but failed to predict accurately when notifications increased in size. As more information deepens our understanding of RRV infection this apparent paradox may come to be explained. Future work aims to refine the model to enable the valid predicting of RRV infection over a broad range of data input values.

Accurate predictions of future outbreaks of RRV infection enable federal, state and local government authorities to implement more effective prevention and control measures. Consequently, research is being conducted to investigate novel ways in which to assimilate the abundance of factors associated with outbreak prevalence into surveillance tools capable of effective forecasting [8,10,27]. Further research is required on RRV seroprevalence in Australia as well as into the seroepidemiological complexities of arboviral outbreaks in general. This may reveal additional novel and exciting statistically resourceful correlations.

5. Conclusion

This study demonstrates an unintuitive application of the examination of seroprevalence data for RRV infection. The linear regression model analysis performed on this limited data set did not validate with sufficient accuracy the use of IgM-positive seroprevalence to predict RRV infection to be of direct benefit to public health stakeholders in its current iteration. However, the predictive analysis did provide qualified evidence for the statistical value of utilising acute sample IgM-positive data for informing best practice in RRV surveillance. Hence, a potential value may exist in gathering pooled seroprevalence data to be harnessed as a means to better inform concurrent surveillance measures, such as for vectors, reservoir hosts and weather conditions, to improve forecasting accuracy and outbreak predictions. We propose that such data could be reported under a third category of *possible* infection. This information may then be catalogued and archived for the primary purpose of enabling the elucidation of potential statistical correlations in future analyses. Due to the inherent problems associated with interpreting IgM-positive serologies, any presumption of RRV infection based on an acute sample result should not be used directly for patient diagnosis and subsequent treatment.

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Authors' Contributions

JBS and AWTR conceived the project. JBS carried out notification data analysis. JBS and NG performed modelling predictions and drafted the manuscript. AWTR supervised the project. NG and AWTR performed statistical checks and critically revised various versions of the paper. All authors contributed to preparation of the final version and agreed to its submission.

Competing Interests

The authors have no competing interests to disclose.

List of Abbreviations

arbo, arthropod-borne; BFV, Barmah Forest virus; CDWG, Case Definitions Working Group (of the Communicable Diseases Network Australia); ELISA, enzyme-linked immunosorbent assay; Ig, immunoglobulin; QLD, Queensland; RRV, Ross River virus.

References

[1] Morens DM, Fauci AS. Emerging infectious diseases: threats to human health and global stability. PLoS Pathog 2013; 9: e1003467.

[2] Cao-Lormeau V-M, Musso D. Emerging arboviruses in the Pacific. Lancet 2014; 384: 1571-1572.

[3] Gubler DJ. Dengue viruses: their evolution, history and emergence as a global public health problem. In: Gubler DJ, Ooi E, Vasudevan S, Farrar J (eds.): Dengue and Dengue Hemorrhagic Fever. Wallingford: CAB International, 2014. pp. 1-29.

[4] Gyawali N, Bradbury RS, Aaskov JG, Taylor-Robinson AW. Neglected Australian arboviruses and undifferentiated febrile illness: addressing public health challenges arising from the 'Developing Northern Australia' Government policy. Front Microbiol 2017; 8: 2150.

[5] LaBeaud AD, Bashir F, King CH. Measuring the burden of arboviral diseases: the spectrum of morbidity and mortality from four prevalent infections. Popul Health Metr 2011; 9: 1.

[6] Ng V, Dear K, Harley D, McMichael A. Analysis and prediction of Ross River virus transmission in New South Wales, Australia. Vector Borne Zoonotic Dis 2014; 14: 422-438.

[7] Tompkins DM, Slaney D. Exploring the potential for Ross River virus emergence in New Zealand. Vector Borne Zoonotic Dis 2014; 14: 141-148.

[8] Heersink DK, Meyers J, Caley P, Barnett G, Trewin B, Hurst T, Jansen C. Statistical modeling of a larval mosquito population distribution and abundance in residential Brisbane. J Pest Sci 2016; 89: 267-279.

[9] Queensland Government. Queensland Joint Strategic Framework for Mosquito Management 2010–2015. Communicable Disease Prevention and Control Unit, Communicable Diseases Branch, Division of the Chief Health Officer. Fortitude Valley: Queensland Health, 2010. pp. 1-26.

[10] Hall RA, Blitvich BJ, Johansen CA, Blacksell SD. Advances in arbovirus surveillance, detection and diagnosis. J Biomed Biotechnol 2012; 2012: 512969.

[11] Lyth A, Holbrook NJ. Assessing an indirect health implication of a changing climate: Ross River Virus in a temperate island state. Clim Risk Manag 2015; 10: 77-94.

[12] Doherty R, Whitehead R, Gorman B, O'Gower A. The isolation of a third group A arbovirus in Australia, with preliminary observations on its relationship to epidemic polyarthritis. Aust J Sci 1963; 26: 183-184.

[13] Hargreaves J, Longbottom H, Myint H, Herceg A, Oliver G, Curran M, Evans D. Annual report of the National Notifiable Diseases Surveillance System, 1994. Commun Dis Intell 1995; 19: 542-574.

[14] Australian Government Department of Health. National notifiable diseases: Australia's notifiable diseases status: Annual report of the National Notifiable Diseases Surveillance System. Available at http://www.health.gov.au/internet/main/publishing.nsf/content/cda-pubs-annlrpt-nndssar.htm. Accessed 5 April 2019; last updated 26 March 2019.

[15] Russell RC. Ross River virus: ecology and distribution. Annu Rev Entomol 2002; 47: 1-31.

[16] Doherty RL, Gorman BM, Whitehead RH, Carley JG. Studies of arthropod-borne virus infections in Queensland. V. Survey of antibodies to group A arboviruses in man and other animals. Aust J Exp Biol Med Sci 1966; 44: 365-377.

[17] Potter A, Johansen CA, Fenwick S, Reid SA, Lindsay MD. The seroprevalence and factors associated with Ross River virus infection in western grey kangaroos (*Macropus fuliginosus*) in Western Australia. Vector Borne Zoonotic Dis 2014; 14: 740-745.

[18] Doherty RL, Standfast HA, Domrow R, Wetters EJ, Whitehead RH, Carley JG. Studies of the epidemiology of arthropod-borne virus infections at Mitchell River Mission, Cape York Peninsula, North Queensland. IV. Arbovirus infections of mosquitoes and mammals, 1967-1969. Trans R Soc Trop Med Hyg 1971; 65: 504-513.

[19] Whitehead RH, Doherty RL, Domrow R, Standfast HA, Wetters EJ. Studies of the epidemiology of arthropod-borne virus infections at Mitchell River Mission, Cape York Peninsula, North Queensland. III. Virus studies of wild birds, 1964–1967. Trans R Soc Trop Med Hyg 1968; 62: 439-445.

[20] Gyawali N, Bradbury RS, Aaskov JG, Taylor Robinson AW. Neglected Australian arboviruses: quam gravis? Microbes Infect 2017; 19: 388-401.

[21] Viennet E, Ritchie SA, Faddy HM, Williams CR, Harley D. Epidemiology of dengue in a high-income country: a case study in Queensland, Australia. Parasit Vectors 2014; 7: 379.

[22] Selvey LA, Donnelly JA, Lindsay MD, Pottumarthy Boddu S, D'Abrera VC, Smith DW. Ross River virus infection surveillance in the Greater Perth Metropolitan area – has there been an increase in cases in the winter months? Commun Dis Intell Q Rep 2014; 38: E114-122.

[23] Knope K, Doggett SL, Kurucz N, Johansen CA, Nicholson J, Feldman R, Sly A, Hobby M, El Saadi D, Muller M, Jansen CC, Muzari OM. Arboviral diseases and malaria in Australia, 2011-12: annual report of the National Arbovirus and Malaria Advisory Committee. Commun Dis Intell Q Rep 2014; 38: E122-142.

[24] Knope KE, Kurucz N, Doggett SL, Muller M, Johansen CA, Feldman R, Hobby M, Bennett S, Sly A, Lynch S, Currie BJ, Nicholson J. Arboviral diseases and malaria in Australia, 2012-13: annual report of the National Arbovirus and Malaria Advisory Committee. Commun Dis Intell Q Rep 2016; 40: E17-E47.

[25] Australian Bureau of Statistics. Queensland Government population projections, 2015 edition. Brisbane: Queensland Government Statistician's Office, 2015.

[26] Kelly-Hope LA, Kay BH, Purdie DM, Williams GM. The risk of Ross River and Barmah Forest virus disease in Queensland: implications for New Zealand. Aust N Z J Public Health 2002; 26: 69-77.

[27] Hu W, Nicholls N, Lindsay M, Dale P, McMichael AJ, Mackenzie JS, Tong S. Development of a predictive model for Ross River virus disease in Brisbane, Australia. Am J Trop Med Hyg 2004; 71: 129-137.