Emerging & re-emerging infectious diseases

0520

A single amino acid substitution in NS5 protein enhances transplacental transmission of Zika virus

C.-F. Qin
Institute of Microbiology and Epidemiology, AMMS, Beijing, China

Background: The emergence of Zika virus (ZIKV) in the Americas has aroused global concern due to its unexpected ability to cause congenital diseases in the context of infection during pregnancy. Previously, we have demonstrated that a single amino acid substitution (S139N) in the prM protein of ZIKV enhances viral neurovirulence and contributes to fetal microcephaly. Yet, how ZIKV crosses the placental barrier to target the fetal brain remains largely unknown.

Methods and materials: Phylogenetic and molecular clock analysis of all ZIKV epidemic strains was performed to identify the newly developed adaptive mutations. Recombinant ZIKV carrying these specific mutations were generated by using standard reverse genetic technology, and characterized with well-established in vitro and in vivo models in comparison with wild type ZIKV. The cytokine profiling was assayed in pregnant mice infected with the mutant virus or wild type ZIKV, and further validated with extensive biochemical assays and animal experiments.

Results: A unique amino acid substitution (M2634V) in the NS5 protein of ZIKV arose in 2014 and stably maintained in the Americas. Additional rounds of adaptive mutations (M3634V, G3460A) resulted in increased viral neurovirulence and transplacental infectivity, and finally led to the emergence of congenital Zika syndrome cases in the Americas.

Conclusion: Our results demonstrate that the adaptive mutation M2634V enhances the vertical transmission of ZIKV by augmenting the secretion of IP-10 during pregnancy. This novel finding, combined with previous results, illustrates the dynamic process how ZIKV gradually acquired multiple adaptive mutations that enhanced viral neurovirulence and transplacental infectivity, and finally led to the emergence of congenital Zika syndrome cases in the Americas.

https://doi.org/10.1016/j.ijid.2020.09.580

0521

What is the best way to diagnose dengue haemorrhagic fever early? Routine application of ultrasound for early detection of dengue haemorrhagic fever


1 District General Hospital Negombo, Centre for Clinical Management of Dengue and Dengue Haemorrhagic Fever, Negombo, Western Province, Sri Lanka
2 District General Hospital Negombo, Paediatrics, Negombo, Sri Lanka
3 Faculty of Medicine, University of Kelaniya, Public Health, Ragama, Sri Lanka
4 District General Hospital Negombo, Centre for Clinical Management of Dengue and Dengue Haemorrhagic Fever, Negombo, Sri Lanka

Background: Dengue is a serious public health burden in Sri Lanka. The dengue illness has two main clinical entities; Dengue Fever (DF) and Dengue Haemorrhagic Fever (DHF). The latter has a transient period of plasma leakage that occurs selectively to pleural and peritoneal cavities. Though less common, DHF is responsible for a large majority of all dengue deaths. Identifying DHF early and managing appropriately can bring down dengue deaths. Most clinical guidelines, identify DHF/Severe dengue by rising haematocrit >20% [World Health Organization (WHO) Guideline on dengue 1997] and ‘warning signs’ (WHO/TDR guideline of 2009). The Centre for Clinical Management of Dengue and Dengue Haemorrhagic Fever (CCMDDHF) routinely used limited Ultrasound Scan (USS), of chest and abdomen, as the most reliable way to identify DHF early.

Methods and materials: Observational study of 400 consecutive serologically verified DHF patients treated during their leaking phase at CCMDDHF since January 2017. All patients had serial USS by trained doctors if their platelet count was below 150,000 (400/400). Data from patient treatment records was extracted onto a data extraction sheet then entered to an Excel database. Descriptive analysis was done using R software.

Results: When DHF was detected through USS, 96% (384/400) did not have haematocrit rise more than 20% from baseline and 64% (256/400) did not have any warning signs. Other indications for
first USS were rising haematocrit above baseline 10.8% (43/400), haemodynamic instability 4.5% (18/400), low urine output 3.2% (13/400), dullness to percussion, reduced breath sounds (clinical suspicion) 7.5% (30/400). Early USS detected DHF in all and showed progressive leaking on serial USS (gradual fluid accumulation). In 90% (360/400) progressive leaking of mild degree (pleural effusion under 2 cm, fluid in Morrison’s pouch, pericholecystic thickening/pericholecystic effusion) was noted while 10% (40/400) had gross leaking (pleural effusion above 2 cm and ascites). 74% (297/400) had progressive leaking to abdomen and 26% (103/400) had leaking into abdomen and chest. None had leaking confined to pleural space.

Conclusion: This study proves routine USS is essential to detect all DHF cases early. Many leak into abdomen, which is clinically undetectable while clinically detectable leaking is gross and progressed.

https://doi.org/10.1016/j.ijid.2020.09.581

0522
Descriptive epidemiology of monkeypox in Nigeria, September 2017–June 2019
S. Akar1,*, Y.-O. Adesola1, S. Akar2, J. Burga3, B. Oluwafemi1, J. Akinrogbie4, C. Ihekweazu5
1 Nigeria Centre for Disease Control, Control and Surveillance and Epidemiology, Abuja, Nigeria
2 African Field Epidemiology Network, NFELTP, Abuja, Nigeria
3 Nigeria Centre for Disease Control, Laboratory, Abuja, Nigeria
4 Nigeria Centre for Disease Control, Programs Coordination and Prevention, Abuja, Nigeria
5 Nigeria Centre for Disease Control, Office of the Director-General, Abuja, Nigeria

Background: Human monkeypox is a rare zoonotic infection caused by an orthopoxvirus and characterized by smallpox-like signs and symptoms. Reported outbreaks have occurred mainly in rural rainforest areas of the Congo basin and West Africa. In September 2017, Nigeria experienced a resurgence of monkeypox. Prior to this, the last of three cases recorded was in 1978. Since then sporadic cases have continued to occur, especially in the Southern part of the country. We present a descriptive epidemiology of monkeypox outbreak in Nigeria from September 2017 to June 2019.

Methods and materials: A retrospective review of monkeypox cases reported to the Nigeria Centre for Disease Control over the period was conducted. Data was cleaned and analyzed for socio-demographic characteristics and signs and symptoms using Microsoft Office Excel version 2010. Counts, frequencies and proportions were determined.

Results: Of 370 suspected cases reported in 30 states, 165 (45.8%) were confirmed in 17 states. Five cases had both monkeypox and chickenpox. Males constituted 115 (70.1%) of cases with mean age of 29.3 ± 11 years. Those most affected were 31–40 years old. 9 deaths were recorded (CFR = 5.5%), 67% in known immune-compromised patients. Case reporting was highest within the first two months of the outbreak; but have continued to occur since then. Most common clinical presentations include rash (all cases), fever (n = 106, 64.8%) and headache (n = 78, 47.3%). Fever preceded rash in 59 (35.8%) of cases. Most common lesions include facial (n = 100, 60.6%), leg (n = 90, 54.5%), head and thoracic (n = 84, 50.9%), and Warthin–Finkeldey (n = 82, 51.4%). Cases were mostly confined to the Southern and Central parts of the country.

Conclusion: Since the largest outbreak of monkeypox in 2017, sporadic cases have continue to occur in Nigeria pointing to endemcity of the disease. Unlike the Central African clade cases are mostly seen in urban dwellers, especially among active young males.

https://doi.org/10.1016/j.ijid.2020.09.582

0523
In search for the hotspots of Disease X: A biogeographic approach to mapping the predictive risk of WHO’s Blueprint Priority Diseases
S. Jagadesh1,*, M. Combe1, M. Nacher2, R. Gozlan1
1 IRD, ISEM UMR226, Montpellier, France
2 Centre hospitalier André Rosemon, Centre d’investigation clinique (CIC Inserm 1424), Cayenne, France

Background: Current trends of emerging infectious disease outbreaks (EIDs) forecast impending global epidemiological crises. Human-driven environmental changes, including climate change along with overpopulation and global travel, have been contributing to EIDs outbreaks in many developing countries. The subject has attracted increasing attention with the recent Ebola and Zika epidemics, which highlights the potential threats to human and animal health, social stability, and global trade and economy. The Blueprint Priority Diseases (BPDs) is a list established by the World Health Organization of ten zoonotic diseases, which are in urgent need of research. We proposed mapping the predictive risk of the BPDs using spatial Bayesian models and species distribution modelling of the outbreaks following the year 2000. The aim is to provide a global perspective, measure predictive risks, and evaluate the use of biogeography on predicting diseases outbreaks. We also proposed disease biogeography as a tool for identifying the potential hotspots for Disease X listed in the BPDs.

Methods and materials: Data of the observed outbreaks (2000–2018) were obtained from promed mail and WHO archives. Bioclimatic covariates and altitude data were extracted from ‘worldclim’ (R package dismo) and the 2017 land cover data (MODIS satellite imagery). We constructed species distribution models including bioclim, maxent and Bayesian models with absence data generated to map the predictive risk of future outbreaks.

Results: Most of the predicted geographic risk extent estimated from the observed data of MERS, Marburg Virus Disease and Rift Valley Fever were found to occur in arid and across the Middle East and Eastern regions of Africa. The predictive extent of Lassa fever and Ebola Virus Disease consisted of regions in the Western and Central Africa, predominated by humid rainforests. We found a significant correlation between the disease extent and the distribution of confirmed and suspected biological reservoirs and also with deforestation. The AUC of the generated models was maintained over 0.9 (average ~ 0.978).

Conclusion: Biogeography is a robust tool in forecasting hotspots of EIDs outbreaks. We will also complete the analysis by aggregating the common risk factors of the predicted EIDs to characterize hotspots for an unknown Disease X.

https://doi.org/10.1016/j.ijid.2020.09.583