Parasite Epidemiology and Control 2 (2017) 50–60

Contents lists available at ScienceDirect

Parasite Epidemiology and Control

journal homepage: www.elsevier.com/locate/parepi

Addressing knowledge gaps in molecular, sero-surveillance and monitoring approaches on Zika epidemics and other arbovirus co-infections: A structured review

Ernest Tambo [a,b,*], Christopher Khayeka-Wandabwa [c,d], Oluwasogo A. Olalubi [e], Ahmed A. Adedeji [f], Jeanne Y. Ngogang [a,g], Emad IM Khater [h,i]

[a] Department Biochemistry, Higher Institute of Health Sciences, Universite des Montagnes, Bangangté, Cameroon
[b] Africa Disease Intelligence and Surveillance, Communication and Response (Africa DISCoR) Foundation, Yaoundé, Cameroon
[c] African Population and Health Research Center (APHRC), Nairobi, Kenya
[d] Health Sciences Platform, School of Pharmaceutical Science and Technology (SPST), Tianjin University, China
[e] Department of Public Health, Kwara State University (KWASU), Malete, Nigeria
[f] Department of Pharmacology, Faculty of Health Sciences, Habib Medical School, Islamic University, Kibuuli, Kampala, Uganda
[g] Service de Biochimie, Centre Hospitalier Universitaire (CHU), Yaoundé, Cameroon
[h] Medical Entomology Department, Faculty of Science, Ain Shams University, Cairo, Egypt
[i] Public Health Pests Laboratory of Jeddah Governorate, Jeddah, Saudi Arabia

ARTICLE INFO

Article history:
Received 4 May 2016
Received in revised form 29 January 2017
Accepted 29 January 2017
Available online 3 February 2017

Keywords:
Zika virus
Arbovirus
Molecular
Diagnosis
Surveillance
Epidemics
Pathogenesis

ABSTRACT

Globalization, with consequent increased travel and trade, rapid urbanization and growing weather variation events due to climate change has contributed to the recent unprecedented Zika virus (ZIKV) pandemic. This has emphasized the pressing need for local, national, regional and global community collaborative proactiveness, leadership and financial investment resilience in research and development. This paper addresses the potential knowledge gaps and impact of early detection and monitoring approaches on ZIKV epidemics and related arboviral infections steered towards effective prevention and smart response strategies. We advocate for the development and validation of robust field and point of care diagnostic tools that are more sensitive, specific and cost effective for use in ZIKV epidemics and routine pathophysiology surveillance and monitoring systems as an imperative avenue in understanding Zika-related and other arbovirus trends and apply genomic and proteomic characterisation approaches in guiding annotation efforts in order to design and implement public health burden mitigation and adaptation strategies.

Contents

* Corresponding author at: Department Biochemistry, Higher Institute of Health Sciences, Universite des Montagnes, Bangangté, Cameroon.
E-mail address: tambo0711@gmail.com (E. Tambo).

http://dx.doi.org/10.1016/j.parepi.2017.01.001

1. Introduction

The observed Zika virus (ZIKV) epidemic among 21st century emerging epidemics continues to ravage and intimidate the affected populations and global community (Petersen et al., 2016a). This has generated panic, fear, and anxiety mainly due to its potential negative consequences on pregnancy and newborn growth (Diagne et al., 2015; Petersen et al., 2016a). Thus, leading to the latest early declaration of "Zika as a public health emergency of international concern" guided by existing evidence from affected populations, potential impact on health and economic in the global community context as pointed by the World Health Organization (WHO) (Diagne et al., 2015; Petersen et al., 2016a). ZIKV belongs to Arthropod-Borne or "Arbovirus" viral diseases and it has become an emergent viral epidemic of public and global health importance since its discovery in Uganda in 1947 (Kean et al., 2015). Global health threat of arboviral diseases or co-infections have been underestimated over time with partially documented morbidity, mortality and disability in most low profile endemic and potentially epidemic terrains. Zika viral epidemics set the pace for worldwide urgency since 2014–2015 in Brazil (Petersen et al., 2016a; Kean et al., 2015). So far, >5000 suspected cases and an estimated >1.5 million at-risk of ZIKV have been documented across the western hemisphere (Caribbean), Africa, Asia-pacific and the Americas (Diagne et al., 2015; Kean et al., 2015; Petersen et al., 2016a).

There is insufficient information on population-based molecular and sero-surveillance approaches alongside longitudinal or cohort molecular and immunological studies. There is an urgent need to establish the link between the spectrum of risk factors of Zika epidemics and/or other arbovirus-vectors and disease transmission dynamics, resurgence and spread, as well as immune status and acquired immune response either locally, regionally or globally (Petersen et al., 2016a; Diagne et al., 2015; Musso et al., 2015a). There is also insufficient indication on previous studies aiming at understanding of the interaction between the *Aedes* vector and pathogen in relation to the exposure frequency and duration and its impact on vector competence, virus abundance, virulence and related severity (Diagne et al., 2015; Kean et al., 2015; Bogoch et al., 2016; Baba et al., 2013). It is well documented that prior viral innate and acquired immune-stimulatory responses play a vital role in subsequent exposure or population protection and defense against foreign pathogens including ZIKV and other related arboviral diseases (e.g.: Dengue virus (DENV), Chikungunya virus (CKHIKV), Yellow fever (YF), Rift valley Fever (RVF), Encephalitis) (Bogoch et al., 2016; Baba et al., 2013; Meister et al., 2008). However, there is need to assess the new Zika virus public health threat in the context of evolving transmission and dual burden with other viral/immunocompromized diseases such as Dengue and HIV/AIDS to measure associated intervention programs effectiveness (e.g. molecular epidemiology approaches) in arbovirus affected countries (Musso et al., 2015a; Papa et al., 2015; Ahmed and Broor, 2014). Moreover, comprehensive quality data and information is required to strengthen local and/or national ZIKV surveillance for preparedness, prevention and improved emergency response capacity, improved integrated vector control programs, management in guiding informed-decision making policies, innovative programs and measuring effectiveness of interventions for effective outcomes and more informed public health choices (Petersen et al., 2016b; Meister et al., 2008; Papa et al., 2015; Kam et al., 2015).

Sero-epidemiologic and molecular virologic approaches along with coherent monitoring systems remain the cornerstone in early detection, prognostic, forecasting, prevention and effective management of patients with immune-depressive viral diseases (e.g.: Zika) or immunodeficiency syndrome (e.g.: HIV/AIDS) over time and space (Baba et al., 2013; Meister et al., 2008; Papa et al., 2015). They are reliable in determining the spectrum of diseases and risk factors, reservoirs, potential route of viral transmission, assessing risk factors and/or determinant dynamics in order to guide operational models implementation in prevention and control (Baba et al., 2013; Meister et al., 2008; Ahmed and Broor, 2014). Nonetheless, most public health laboratories in arbovirus endemic areas are poorly-equipped in delivering routine screening service to vulnerable populations. Thus, in absence of such infrastructures, routine or active laboratory viral detection and diagnostics or confirmation and reporting in Arbovirus incidence and prevalence are not performed (Musso et al., 2015a; Baba et al., 2013; Ahmed and Broor, 2014; Kam et al., 2015). Often, where the assays exist, they are only done on very few financially wealthy "patients" who can afford the high cost of currently available molecular techniques (Meister et al., 2008, Papa et al., 2015, Tambo et al., 2014b, Pauvolid-Corrêa et al., 2015). The exception is on HIV/AIDS; almost free screening benefits from government subsidies and PEPFAR sponsored projects in some African countries. It is thus clear that most viral diseases are undetected and underestimated in most of these countries with sometimes a high level of sub-threshold viral burden (e.g.: seropositivity) and potential misdiagnosis due to cross-reactivity owing to varied degree of acquired immunity either from same quiescent infections, concurrent co-infections or epidemics in the region (Musso et al., 2015a, Papa et al., 2015, Tambo et al., 2014d, Pauvolid-Corrêa et al., 2015, Yeon-Hee et al., 2015, Andayi et al., 2014).

This structured review paper assesses the nature and type, extent of applicability and effectiveness of sero-epidemiologic, molecular surveillance and monitoring system applications for ZIKV epidemics and other arboviral diseases for clinical profiling/

mapping and identification of risk factors for prevention and control. Providing data-driven insights is essential in moving forward ZIKV research and development, translation research into innovative response approaches.

2. Methods

2.1. Structured literature review

In order to better characterize the nature, type and extent of applicability of sero-epidemiologic and molecular monitoring and screening techniques on ZIKV and related arboviral co-infections globally, a structured literature review from the previous 16 years (Jan 2000–March 2016)using the terms "molecular or serology approaches in Zika virus and arbovirus co-infections" was conducted using Google Scholar in March 2016. Additional publications were identified from references of retrieved articles as well as PubMed, EMBASE, Cochrane and MEDLINE electronic database and relevant grey literature. The period approximately represents over a decade of high throughput translational research on arbovirus surveillance, improvement of diagnostics precision in terms of sensitivity, specificity and unit cost in addition to the enhanced search for chemotherapy including vaccines (Rubio et al., 2010; Weaver and Reisen, 2010; Hadler et al., 2015; Liang et al., 2015). Articles directly pertaining to quantitative measurement or detection techniques for ZIKV, flavivirus and arbovirus co-infections using molecular and serological approaches, articles reporting the validity of the molecular and serology methodology, and articles that have used varied bioassay measurement methods to determine the prevalence of ZIKV and co-infections and/or validate case reports alongside associated risk factors were considered (Monath et al., 1973; Kam et al., 2015).

Structured literature review provided the capacity to systematically identify prominent themes and concepts with content analysis (Webster and Watson, 2002; Higgins and Green, 2008). Google Scholar (http://scholar.google.com) is an appropriate tool for this approach given the wide scope of disciplines that may document flavivirus, ZIKV or arbovirus co-infections serology or molecular approaches alongside associated sensitivity, specify and validation. Google's search engine is also readily accessible to researchers, healthcare experts and policymakers seeking information. Further, Google's proprietary natural language search algorithm indexes and analyzes results from across all available online academic databases, and produces equivalent results to other databases for meta-analysis (Aguillo, 2011).

Search details for potential papers alongside ranking in order of relevance by the search algorithm are shown in Fig. 1. Few studies met the inclusion criteria due to heterogeneity in approach and tools, human or animal targets, local or national single or integrated vector control programs, molecular, sero-epidemiologic and immunologic methods, and management of arboviral diseases. A data extraction form was developed to capture all data on nature, extent, geographical location and potential impacts/consequences of various types of arthropod-borne diseases epidemics and type of interventions over time (results are herein tabulated). Also, documentation of public health burden of ZIKV complications or pathophysiologic symptoms was done in

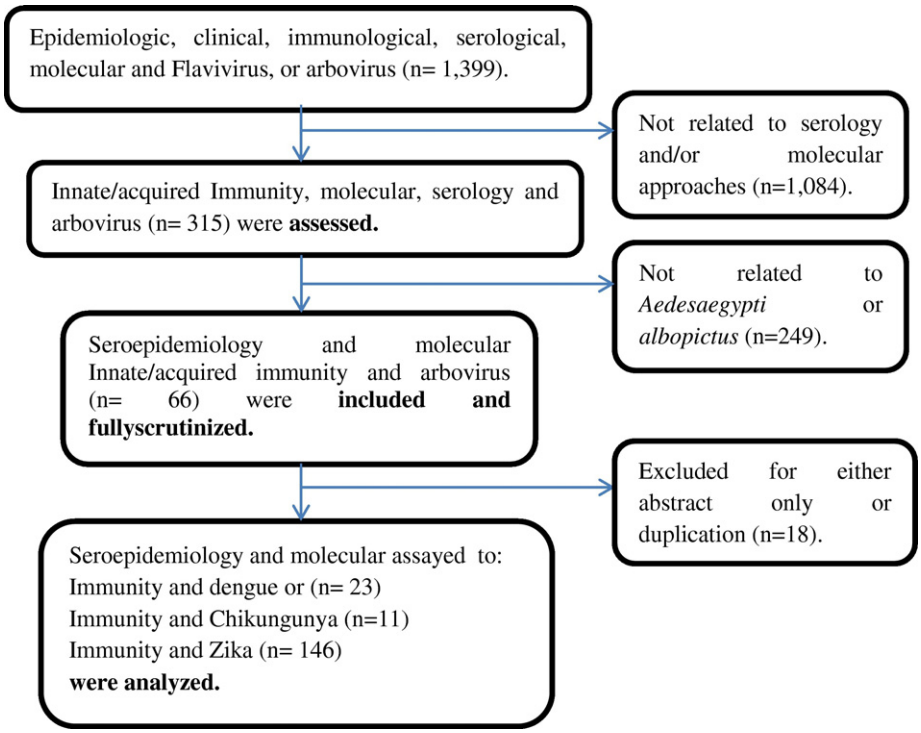

Fig. 1. Summary literature search on immunity and arbovirus worldwide.

affected patients, incidence, prevalence and fatality rate in relation to molecular, sero-epidemiologic and immunologic profile of studied populations over time.

3. Results

Our results of systematic literature search showed that 315 papers and reports were eligible for assessment. Post-evaluation only 66 met the inclusion criteria and were fully scrutinized, of which 40 full peer-reviewed papers on ZIKV were included in the final analysis (Fig. 1).

3.1. Global emerging Zika and other arboviral diseases key characteristics

Key characteristics and information on Zika and other (arthropod-borne) arbovirus diseases worldwide are as presented. Our results showed the variations in emerging and re-emerging arboviruses systematic and sporadic distribution from diverse *Aedes* mosquito species in Africa, Americas and Asia-Pacific regions. Our findings of human and other vertebrate's seroprevalence attesting this geo-distribution and patterns are also documented mainly in the tropic and subtropic zones, but rapid spread into new territories (Table 1).

From the presented range of arbovirus epidemiologic dynamics, it is evident, ZIKV clinical signs and symptoms could easily be mistaken for dengue (DEN) or Chikungunya (CHIKV) fevers. It is also clear from result presented that, *Aedes aegypti* and *Ae. albopictus* are among the main vectors transmitting ZIKV, DEN or CHIKV as well as eliciting global public health importance as

Table 1
General Key characteristics and information on Zika and other (arthropod-borne) arboviral diseases worldwide.

Arbovirus Disease	Arthropod vector	Arthropod Virus subtype	Incubation period, days	Complications symptoms	Region Epidemics, year(s)	Incidence	Prevalence	Fatality rate
Zika viral fever	*Aedes aegypti* & *A. albopticus*	Zika virus (ZKV1,2,3)	3–7	Conjunctivitis and joint pain, mother to the baby during pregnancy with microcephaly neurologic and birth defects, Guillain–Barré syndrome syndrome and other poor birth outcomes of babies	Africa, Southeast Asia and the Pacific Islands, 1954, Central and South America and the Caribbean,	-NA	1.5 million	NA
Dengue hemorrhagic fever Dengue fever	*Aedes aegypti*& A *albopictus*	Dengue virus (DENV1,2,3,4)	2–14	Shock, internal bleeding, and organ damage	Tropical and subtropical regions 1800s,	<284–528 million infections annually	>652,212 DHF 67–136 million DF	<1% with treatment, 1–5% without; about 25% severe cases
Chikungunya fever	*Aedes aegypti* or *A. albopictus* mosquitoes	Chikungunya virus	3–7	Severe and disabling, Joint and muscle pain, joint swelling, or rash	Africa, Asia, Europe, and the Pacific islands, The Americas on islands in the Caribbean	NA	NA	
Rift valley Fever	*Culex tritaeniorhynchus* and *Aedes vexans*	Rift valley virus	2–6	Hemorrhagic fever, meningo-encephalitis	Eastern, Southern, and Western Africa	NA	NA	1% in humans; in pregnant livestock, 100% fetus fatality rate
West Nile fever	West Nile virus	*Culex* mosquitoes	2–15	Swollen lymph nodes, meningitis, encephalitis, acute flaccid paralysis	North America, Europe, West and Central Asia, Oceania, and Africa, 1937	NA	NA	3–15% in severe cases
Yellow Fever	YF virus	*Aedes aegypti* mosquitoes	3–6	Jaundice, liver damage, recurring fever, gastrointestinal bleeding,	Tropical and subtropical regions of South America and Africa, 1937	NA	NA	3% in general; 20% chronic cases
Japanese encephalitis disease	Japanese encephalitis virus	*JEV1,2,3,4,5*	5–15	Encephalitis, seizures, paralysis, coma, and long-term brain damage	Southeast and East Asia	NA	NA	20–30% in encephalitis cases

suggested by their global distribution pattern. Despite this global knowledge and inherent appreciation of epidemic threat that would emerge in the event of an outbreak especially in Africa where ecological determinants are ripe, our search results confirms that incidences and prevalence profiling in Africa remains patchy and sparse as compared to other regions known to be equally potential to outbreaks and epidemics. Similarly, despite the disproportionate prevalence profiling, it is apparent that local clinicians in Africa and most diagnostic laboratories are more conversant with DENV and CHIKV. In contrast, few physicians are clinically at ease, well versed or aware of ZIKV clinical cues especially when complicated with potential for CHIKV/DENV and few laboratories test for clinical infection. Consequently, most ZIKV infections are probably missed or misdiagnosed due to DENV, CHIKV and other infectious diseases cross-reactivity. However, there was little information from the literature review process on early detection and local laboratory monitoring gaps to inform ZIKV threat, prevalence and epidemics. Local and global funding commitment should be directed to strengthening Zika virus epidemiologic and laboratory surveillance capacity and capability of resource-limited countries, cost-effective, rapid and field-adaptable molecular and serological diagnostic kits tests validation, accessible and available to high risk populations mainly pregnant women attending antenatal clinics in primary healthcare, collaborative regional and global surveillance and control network and strategies against circulating *Aedes* and Zika virus diversity, Zika epidemics preparedness and rapid response surge capacity in *Aedes* prone countries mainly Africa.

3.2. Understanding time-bound detection methods impact on Zika and other arboviral diseases on vulnerable populations

Arboviruses have over time gained a unique standing among viruses due to their biological transmission mode involving the virus, vector and vertebrates beside other abiotic and biotic factors. Understanding the nature, extent and impact of population immunity in emerging Zika epidemics and other arbovirus fetal, childhood and maternal burden is vital in elucidating the contextual knowledge and practices on co-infections. Our finding showed that very little is documented in the sero-surveillance and molecular profiling of ZIKV among varied endemic or epidemic prone-settings in Africa with much insight information originating from Europe, Asia and America (Table 2a).

Still, similar findings showed that there are sparse data on the sero-epidemiology of dengue and Chikungunya on the level of immune and other molecular related modulators of clinical course relevance particularly in Africa. Most applications have been in the context of case reports and few in population-based serologic surveillance. The small-scale utility of the serology and molecular techniques would be the outstanding limitation for appraising possible capacity and cost benefit analysis in replicating the same on a larger scale. Equally, due to the close association of clinical symptoms between arboviral infections and the challenging application of serology alone owing to false positive antibodies and antigens cross-reactivity vis-a-vis high cost and time consuming RT-PCR assays, complex possible combination or preferential application of either of the two diagnostic approaches such as ultra-neurosonographic/Laser detection and diagnosis of microcephaly, fetal brain malformations and anomalies. Even so specific, rapid and sensitive molecular monitoring and surveillance kits (e.g. RT-PCR) for detection of ZIKV and other arboviral infections in the early stage of infection and the relay of results could be key to immediate clinical intervention decision unlike serological profiles assessment. Additionally, molecular approaches have the capacity to utilize less invasive samples like urine and Saliva, unlike some serology techniques that will be sample specific for instance wanting to utilize serum whose collection involves an invasive process (Table 2b).

From in-depth assessment of the literature collated, a combination of molecular and serological surveillance approaches have been applied in recent ZIKV epidemics in South American regions with more researchers and/or publishers encouraged to adhere to open access and data sharing policy on Zika knowledge exchanges and education. Our review has confirmed a combination of serology, biochemical and RT-PCR or RT-PCR alone as the most robust approach with capacity to utilize non-invasive and less laborious sample collection techniques hence more befitting for population based surveillance, infants and newborns.

3.3. Establishing effective molecular and immunological surveillance and monitoring in resource-limited countries

Examining bodily fluids samples in early quantification and detection of antibodies and/or antigens, cellular systems, cytokines and other molecular aspects is critical in understanding the disease course and important functional mechanisms in protection and defense against arboviral diseases. However, the detection and diagnostics methods are absent or not evenly establishing in most laboratory daily routine performance in most resource-limited countries found in sub-Sahara Africa. Our finding showed that, in >50 Zika-prone and over 100 dengue-prone countries less than a quarter performed routine laboratory bodily fluids testing or screening, whereas another quarter were performing periodic annual sentinel checks such as the America, Australia, UK, China and Uganda.

The urgent need to establish a functioning sero-epidemiological and molecular surveillance and monitoring systems in laboratory or epidemiologic surveillance is advocated in arboviral and other emerging viral diseases epidemics settings. Several detection and diagnostics methods and tools were reported in sero-epidemiologic, virologic and molecular investigative techniques in blood or bodily fluids examinations including ELISA, polymerase chain reactions, neutralization test, complement fixation and hemagglutination-inhibition testing. Understanding immune response with age and unprotected/partially immune people, mainly pregnant women, fetal and placental tissue/fluid examination during the first trimeter and throughout gestation, could provide some further clues. Moreover, there is need to assess the impacts of co-infections or super-infections on Zika epidemics and other diseases pandemic such as HIV/AIDS or other immunodeficiency disorders. The precedence being much is still to be done in term of operational research and development towards innovative and more sensitive, real time and cost-effective diagnostics approaches and tools including existing diagnostics RT-PCR or ELISA/IFA assays. Addressing the most pressing knowledge,

Table 2
Key molecular and serological assessment approaches and techniques in Zika and other arboviral infections

a. Serological and molecular approaches for Zika and arboviruses post infection and unique observations

Arbovirus type, sample size of people screened (n) and infection context	Molecular and/or Serology marker assays performed	Window period within which the marker was detected	Unique observations
Zika Virus ($n = 11$) Yap State, Micronesia Epidemic (April 2007)	MAC/ELISA for IgM and capture ELISA for IgG with whole viral antigen and monoclonal antibodies.	IgM-3 days after onset of symptoms. IgG-appear after day 10.	Rapid laboratory assay suggested that a dengue virus (DENV1-4) was the causative agent. IgM can persist over a longer period hence not precise predictor marker. RT-PCR demonstrated ≈90% nucleotide identity with ZIKV indicating ZIKV was the causative agent of the Yap epidemic.
Zika virus ($n = 1$) Australian woman after a 9-day holiday to Jakarta, Indonesia.	Investigations at this time showed a total leukocyte count of 3.6×10^9 cells/L (reference range = 4.0–11.0 $\times$ 10^9 cells/L), a hemoglobin level of 137 g/L (reference range = 115–150 g/L), a hematocrit of 39%, and platelet count of 230×10^9 cells/L (reference range = 140–400 $\times$ 10^9 cells/L). Reactive lymphocytes were present on a blood film while baseline liver and renal function test results were normal.	Examination on day 5 of illness.	Dengue serologic analysis on day 5 of her illness showed a positive result for IgG, a weakly positive result for IgM, but a negative result for nonstructural protein 1 (NS1 antigen) by enzyme immunoassay. A generic flavivirus group polymerase chain reaction (PCR) result was positive, and the patient was provisionally given a diagnosis of dengue fever. A dengue-specific PCR result was negative. Sequencing of the original flavivirus PCR product identified it as Zika virus (GenBank accession no. KF258813).
Zika virus ($n = 2$) A married couple from Italy in their early 30s after their return from a holiday trip to French Polynesia (December 17, 2013 to January 4, 2014). Serum samples of the acute and convalescent phase and heparinized, whole blood samples for Serological and virological assays	The man showed leukopenia (4300 cells/L, reference values 4800–10,800/L), monocytosis (15%, reference value 0–12%) and thrombocytopenia (139,000/L reference values 140,000–440,000/L). The woman had a normal full blood count. Transaminases, creatinine, and erythrocyte sedimentation rate were normal in both patients.	3 days after arrival	In view of the accompanying symptoms and the travel history to French Polynesia during the ongoing ZIKV outbreak, an acute ZIKV infection was suspected.
	ZIKV–RT-PCR for the female was + ve and − ve for the man	Samples assay at 3 days after return.	Only the female partner was positive confirming the need for more evidence on sexual transmission.
	IgG and IgM seroconversion against ZIKV, by indirect immunofluorescence assay	Day 3, 35 and 62	Indirect immunofluorescence assay (IIFA) and ELISA was positive for dengue (Anti-DENV-IgG & Anti-DENV-IgM) on day 35 while for zika virus, Anti-ZIKV-IgG and Anti-ZIKV-IgM was only positive on IIFA on the same day 35 for the female. IIFA for zika Anti-ZIKV-IgG and Anti-ZIKV-IgM was also positive on day 35 for the man despite the man being –ve of zika virus through ZIKV-RT-PCR. Hence attesting the need to synergize immunoassay with RT-PCR as confirmatory test.
	Multiparameter flow cytometry immunological assays-Quantification of leukocyte populations in healthy control samples and Zika patients; mDCs, B cells, T cells, CD4T, CD8T, Naïve CD4, Memory CD4, Naïve CD8 and memory CD8	convalescent phase	No abnormality in ZIKV patients compared to healthy controls.
	Antigen uptake capacity of DCs, using fluorescent FITC-dextran beads as surrogate antigens.	convalescent phase	To determine the functionality of blood DCs in convalescent ZIKV patients compared to healthy controls-The blood DCs from ZIKV patients were established to equally effective for antigen capturing than DCs from healthy donors. This observation is achieved despite the

(continued on next page)

Table 2 *(continued)*

a. Serological and molecular approaches for Zika and arboviruses post infection and unique observations

Arbovirus type, sample size of people screened (n) and infection context	Molecular and/or Serology marker assays performed	Window period within which the marker was detected	Unique observations
			fact that, dendritic cells (DCs) are primary infection targets for most mosquito-borne flaviviruses,
Zika virus ($n = 6$) and healthy controls ($n = 20$): Patients had acquired ZIKV infection in Southeast Asia, Polynesia, or Brazil	ACUTE PHASE-Significant concentration elevation for interleukin (IL)-1b, IL-2, IL-4, IL-6, IL-9, IL-10, IL-13, IL-17, as well as for interferon-γ-induced protein 10 (IP-10), regulated on activation, normal T cell expressed and secreted (RANTES), macrophage inflammatory protein 1 alpha (MIP-1a) and vascular endothelial growth factor (VEGF), when compared to healthy blood donors. RECOVERY PHASE - significant increases demonstrated in the levels of IL-1b, IL-6, IL-8, IL-10, IL-13, IP-10, RANTES, MIP-1a, MIP-1b, VEGF, fibroblast growth factor (FGF), and granulocyte-macrophage colony stimulating factor (GM-CSF) as compared with healthy controls.	Serum samples were classified as either acute (taken ≤10 days after symptom onset) or recovery (taken >10 days after disease onset).	Interferon-γ (IFN-γ) showed a non-significant increasing pattern in both acute and recovery phase. Tumor necrosis factor-α (TNF-α) concentrations had a non-significant median increase during the acute phase. Majority of the cytokines and factors elevated in the acute phase showed a tendency to return to normal levels in the later recovery phase. In both the acute and recovery phase, no significant changes could be observed for IL-1ra, IL-5, IL-7, IL-12, monocyte chemotactic protein 1 (MCP-1), eotaxin, and platelet-derived growth factor-bb (PDGF-bb).
Acute ZIKV infection ($n = 1$). In a German traveler returning from Malaysian Borneo. On September 1, 2014, a 45-year-old woman was seen in an outpatient clinic in Heidelberg for fever of up to 39 °C and maculopapular rash covering her trunk, arms, and legs.	6 days after returning: Laboratory analyses showed: Slightly elevated C-reactive protein level at 5.2 mg/L (reference range < 5.0). Liver function test and complete blood count results were within reference range. An indirect immunofluorescence assay for dengue virus demonstrated an IgG titer of 1:80 and no IgM (cutoff <1:20). Three days later: There was no lymphadenopathy but indirect immunofluorescence assay for ZIKV demonstrated an IgM titer of 1:640 and an IgG titer of 1:320 (cutoff <1:20). Day 11 ZIKV serologic testing: a decreased IgM titer of 1:160 and an increased IgG titer of 1:2560. Viral neutralization testing	6 days after she had returned from a 3-week vacation (within which the clinical symptoms were observed) and subsequent assays to day 11.	Chikungunya virus serology results were negative at day 11. There was a decrease in IgM titer by day 11. The viral neutralization testing demonstrated the presence of ZIKV-specific neutralizing antibodies.

b. Comparator review summary on ZIKV infection context/clinical onset time frame and detection in analyte of choice

Serum:	ZIKV can be detected in serum typically up to 3–5 days after the clinical onset; the viral load seems to peak when clinical signs appear.
Saliva:	ZIKV can be detected in saliva but not longer than the days prescribed in serum after clinical onset.
Urine and Semen:	The viral load will be higher than in blood with a peak between days 5–7 in urine. Equally, detection of the virus using semen as diagnostic aliquot have been reported but with no specification whether at acute or recovery phase.
Molecular methodology approach guiding facts:	Molecular testing-PCR based: Blood samples, urine and saliva for Real Time Polymerase Chain Reaction (RT-PCR) assays viral load detection appears to last up to 20 days after clinical onset. To diminish the risk of missed opportunities, a combination of molecular approaches serum Amniotic fliud and saliva or urine is defined as ideal especially if veracity of time of clinical onset cannot be clearly established. Equally, the combination of urine and saliva is evidently more robust at any stage of clinical onset. The less invasive modes of urine and saliva are suitable for infants and newborns. In situations of high reliance on serologic approaches alone without incorporating molecular approaches through RT-PCR with flavivirus consensus primers there is high like hood of cross-reactivity with dengue virus antigens hence mis-diagnosis for dengue instead of ZIKV.

[a,b](Lanciotti et al., 2008; Charrel et al., 2016; Zammarchi et al., 2015b; Charrel et al., 2016; Kwong et al., 2013; Tappe et al., 2015a; Tappe et al., 2015b; Buathong et al., 2015; Haddow et al., 2012; Pyke et al., 2014; Faye et al., 2013; Zammarchi et al., 2015a; Shinohara et al., 2016; Musso et al., 2015b; Musso et al., 2015c).

laboratory and clinical capacity and capability needs of Zika virus vulnerable countries requires investing in implementing rapid, sensitive, and specific Zika and other arboviral diseases tools for early detection and surveillance (serological and molecular validation), extensive operation and epidemiological research data consolidation and translation for evidence gaps response, with focus on neonatal, child-maternal health; deciphering climate change and globalized travel and trade, and annual mass gathering pilgrims on Zika genomic diversity and evolution pattern, virulence acquisition, emergence and geographical spread.

3.4. Strengthening local and national integrated "One Health" surveillance and rapid response systems

Elucidating the susceptibility and spread patterns of Zika epidemics and other arboviral diseases in developing countries is imperative in establishing the most effective solutions to deal with the vectors source and local competence. Even though this paper was not aimed at evaluating surveillance and "One Health" implementation barriers and issues, Zika epidemics, Chikungunya and dengue resurgence have showed the challenges and issues of existing within Arbonet and DengueNet platforms and framework. There is an increasing need to leverage on novel cost-effective and scalable technological approaches on mosquitoes-transmitted diseases "One Health" surveillance framework and action plans adoption. National/regional infectious diseases priorities alignment with integrated "One Health" surveillance and framework implementation holds great opportunities in understanding *Aedes*-linked human-animal and environment interface towards better, forecasting, early waning indicators in effective and efficient prevention and response to local and international emerging Zika and other future arbovirus threats and epidemics or disasters crises.

4. Discussions

This review paper showed that ZIKV infections share similar early signs and symptoms with other arbovirus with indications that physiopathological complications associated with ZIKV would be deleterious to fetal development as well as threat to motherhood. Health professionals in most developing countries including Africa lack appropriate knowledge and skills for, timely and practical Zika diagnosis and management, adequate preparedness and rapid emergency response relay to their communities (Tambo et al., 2014 & 2016a; Kwan et al., 2012; Monath et al., 1980; Robin and Mouchet, 1974). All these coupled by wide flora, fauna, the good temperatures and climate in most African contexts where the pathogens originated and/or are known to exist in pockets, provides a befitting niche for endemicity and sporadic outbreak based on the inherent favorable ecological factors (Carver et al., 2009; Kuno and Chang, 2005; Kraemer et al., 2015). To date, epidemic episodes have not been the case in Africa but equally, in case of an outbreak there is limited guiding content on possible serological and other molecular markers arrays to enhance real time epidemiological vigilance (Zammarchi et al., 2015a; Charrel et al., 2016; Faye et al., 2013). Equally, knowledge of the immune-modulatory and molecular dynamics that would enhance indepth understanding of the virus pathogenesis and presence or absence of observed differential diagnosis is splintered among diverse sub disciplines (McFarlane et al., 2014; Kam et al., 2015; Kuno and Chang, 2005; Hegde et al., 2015). The above context linked with insights from existing grey literature and published findings guided by previous studies have shown that in sylvatic transmission cycle, human host carrier or reservoir or non-human intermediate or incidental host may harbor varied degree of viraemia depending on the innate and acquired immunity over time. Moreover, the highly intertwined host-pathogen interaction via favorable abiotic and biotic process ascribed in the context of such infectious pathogens like Zika with far reaching incubation period clinical symptoms ranging from few days to 1 week or there about, would point to emerging complexity in public health control and management (Tambo et al., 2016b; Fine et al., 2011; Kuno and Chang, 2005). Thus, inclusive consideration of the diverse findings would help elaborate the varying epidemic trends between Africa and the Americas in the context of prevailing abiotic and biotic factors. Nevertheless, comprehensive research is needed to study and establish any link between Zika microcephaly, hydrops fetalis, arthrogryposis and hydranencephaly to stillbirth vis-à-vis the pathogen underlying molecular principles and pathognomy (Petersen et al., 2016b; Christofferson and Mores, 2015; Hegde et al., 2015; Zammarchi et al., 2015a; Kuno and Chang, 2005). Furthermore, to examine the role of immunomodulation associated molecular and immune-resilience markers that can either demonstrate to be relevant diagnostic parameters and/or enhance possible severity or tolerance against ZIKV and other arbovirus pathogens (Diagne et al., 2015; Ginier et al., 2016; Meister et al., 2008; Faye et al., 2013; Charrel et al., 2016). It is in view of the fact that transmission dynamics and contextual determinants for epidemic are highly potent especially in Africa yet possible indicators or predictor markers still required further validation as valuable tools in surveillance and epidemic ensnare especially in Africa (Musso et al., 2015a; Hegde et al., 2015; McSweegan et al., 2015; Tappe et al., 2015b; Weaver and Forrester, 2015; Lanciotti et al., 2008; Haddow et al., 2012; Faye et al., 2013).

From our results, latter (RT-PCR) also demonstrated to have high sensitivity and specificity threshold (Medina et al., 2015; Zink et al., 2015; Tappe et al., 2015a; Zammarchi et al., 2015a; Lanciotti et al., 2008). Though the techniques have not been widely used in the African context as compared to Europe, USA and Asia, applicability and viability has been partially assessed in Africa in varying scenarios (Gasque et al., 2015; Blair and Olson, 2015; Kleinman, 2015; Faye et al., 2013). Nonetheless, the approaches have adhered to robust methodologies with the capacity to inform on cues of averting cross-reactions for instance mis-diagnosis between dengue and Zika virus subtypes (Diagne et al., 2015; Ginier et al., 2016; Musso et al., 2015a; Peterhans et al., 1999; Kleinman, 2015; Zammarchi et al., 2015a; Faye et al., 2013; Lanciotti et al., 2008). Three techniques have been used broadly; indirect immunofluorescence assay (IIFA), Enzyme linked immunosorbent Assay (ELISA) and RT-PCR or next generation sequencing (NGS) (Kean et al., 2015; Musso et al., 2015a; Papa et al., 2015; Robin and Mouchet, 1974; Tappe et al., 2015b; Weaver and Forrester, 2015; Haddow et al., 2012; Pyke et al., 2014; Faye et al., 2013). Multiparameter flow cytometry has had marginal application yielding less insightful results between the cases and controls (Weaver and Forrester, 2015; Peterhans et al., 1999; Zammarchi et al., 2015a).

Immunoassay techniques have majorly targeted IgM, IgG, cytokines and chemokines. Full blood count as well as liver and renal functions tests have been major baselines assays in majority of articles (Buathong et al., 2015) and previous cases reviewed but their outputs did not serve as compelling pointers to any arbovirus prediction due to the readings being within or almost within reference ranges regardless of the pronounced clinical symptoms indicating possible arbovirus infection (Weaver and Forrester, 2015; Zink et al., 2015; Zammarchi et al., 2015a; Buathong et al., 2015; Haddow et al., 2012; Zammarchi et al., 2015b; Kwong

et al., 2013). The predictive value of the different assays utilized varied, and a combination of techniques sharply showed a clear contrast on specificity, sensitivity and reliability of different molecular and serological applications (Medina et al., 2015; Weaver and Forrester, 2015; Diallo et al., 2014; Haddow et al., 2012; Lanciotti et al., 2008; Zammarchi et al., 2015a). For instance, a combination of serology (as an initial diagnostic methodology) and molecular approach as a second step confirmatory test proved to be more robust than utilization of only one serology approach or a combination of various serology dimensions (Sow et al., 2016; Kirya et al., 1977; Monath et al., 1980; Robin and Mouchet, 1974; McSweegan et al., 2015; Lanciotti et al., 2008).

Despite the potential to optimize the technique, practical steps to actualize applicability remain scarce. First, the developed nations have reference laboratories and/or satellite sample collection centers in strategic sites linked to the reference laboratory with well-equipped personnel skill wise and resources where the public can readily access guidance for rapid response (Zammarchi et al., 2015a; McFarlane et al., 2014; Hegde et al., 2015). Such threshold of preparedness is widely lacking in Africa (Laperriere et al., 2011; Kirya et al., 1977). The threshold of evidence on host immune status, sero-epidemiological genetic and ecological drivers of Zika-associated epidemics as well as knowledge of their vectors' regional distribution and evolving trends remains patchy and scarce (Tambo and Xiao-Nong, 2014; Laperriere et al., 2011; Wauquier et al., 2010).

From the collaborated evidence it is clear that ZIKV-RT-PCR has the desired specificity and sensitivity for detection on applicable flavivirus based on clinical symptoms observed (Robin and Mouchet, 1974; Hegde et al., 2015; Weaver and Forrester, 2015; Faye et al., 2013; Lanciotti et al., 2008). In its enhancement and scaling up as a screening technique, complementing more funding and investment in novel, safe and efficacious therapeutics agents and vaccines in meeting the vulnerable population and travel medicine immunization programs hopes and needs will be of immense benefit to cases profiling and management (Chang et al., 2015; Abraham et al., 2015; Petersen et al., 2016b).

For a holistic translational research approach, elucidating and mapping the functional and cellular impacts of Zika and other emerging/re-emerging arbovirus epidemics and resurgence, innate or acquired immune impairment pattern, immune responses and status of both unprotected and partially protected populations' adaptations in guiding innovations in therapeutics and immunizations models desires more focus (Gasque et al., 2015; Blair and Olson, 2015; Salje et al., 2012; Vazquez-Prokopec et al., 2010). Research and Development (R&D) towards informed integrated vector prevention and smart management priorities and strategies is imperative in advancing Zika and related flavivirus infections or concurrent co-infections. Such efforts will importantly, foster sustained and resilient local and regional *Aedes* linked Zika infection surveillance data and indicators, early warning and modeling systems for proactive evidence-based decision policy and emergency preparedness and response performance and effectiveness (Eppes et al., 2017).

5. Conclusions

There is a pressing need to develop more sensitive, low-cost point of care and field adaptable rapid diagnostics and confirmation kits for Zika epidemics and related arboviral infections in zoonose-prone settings or vulnerable countries for prompt response interventions. Among all molecular, immunological and biochemical markers assessed in relation to related techniques applied in various studies/findings and captured in the presented findings, real time polymerase chain reaction would be more pragmatic molecular approach in terms of precision, specificity and sensitivity. However, the unit cost of setting up the resource and availability of desired reagents, associated refill costs and skill capacity may require more cost benefit analysis and need assessment from health economics and biomedical perspective as well as exploring industrial and end user partnerships through either regional health blocks or governments to advocate for subsidies and related sustainability. The possible cost effectiveness burden was notable from the sturdiness of methodologies applied in papers reviewed and proportion of only few samples that would be analyzed as compared to scenarios in which other techniques were utilized. Moreover, strengthening effective and reliable local, national and regional quality integrated surveillance data and contextual knowledge in guiding evidence-based early warning is crucial in supporting long-term robust community-based programs, public health laboratory monitoring systems and scaling up informed integrated vector control platforms.

Competing interests

The authors have declared that they have no competing interests.

Authors' contributions

ET conceived the idea. ET and CKW extracted literature data, prepared the initial draft of the manuscript, assessed and analyzed the data. ET, CKW, OAO, AAA, JYN and EIMK provided addition information. All authors read and approved the final manuscript.

Acknowledgements

This work was not supported by any funders.

References

Abraham, R., Mudaliar, P., Jaleel, A., Srikanth, J., Sreekumar, E., 2015. High throughput proteomic analysis and a comparative review identify the nuclear chaperone, Nucleophosmin among the common set of proteins modulated in Chikungunya virus infection. J. Proteome 120, 126–141.

Aguillo, I.F., 2011. Is Google Scholar useful for bibliometrics? A webometric analysis. Scientometrics 91, 343–351.

Ahmed, N.H., Broor, S., 2014. Comparison of NS1 antigen detection ELISA, real time RT-PCR and virus isolation for rapid diagnosis of dengue infection in acute phase. J. Vector Borne Dis. 51, 194.

Andayi, F., Charrel, R.N., Kieffer, A., Richet, H., Pastorino, B., Leparc-Goffart, I., Ahmed, A.A., Carrat, F., Flahault, A., De Lamballerie, X., 2014. A sero-epidemiological study of arboviral fevers in Djibouti, Horn of Africa. PLoS Negl. Trop. Dis. 8, e3299.

Baba, M., Logue, C.H., Oderinde, B., Abdulmaleek, H., Williams, J., Lewis, J., Laws, T.R., Hewson, R., Marcello, A., D'agaro, P., 2013. Evidence of arbovirus co-infection in suspected febrile malaria and typhoid patients in Nigeria. J. Infect. Dev. Ctries. 7, 051–059.

Blair, C.D., Olson, K.E., 2015. The role of RNA interference (RNAi) in arbovirus-vector interactions. Viruses 7, 820–843.

Bogoch, I.I., Brady, O.J., Kraemer, M.U., German, M., Creatore, M.I., Brent, S., Watts, A.G., Hay, S.I., Kulkarni, M.A., Brownstein, J.S., Khan, K., 2016. Potential for Zika virus introduction and transmission in resource-limited countries in Africa and the Asia-Pacific region: a modelling study. Lancet Infect. Dis. 16 (11), 1237–1245.

Buathong, R., Hermann, L., Thaisomboonsuk, B., Rutvisuttinunt, W., Klungthong, C., Chinnawirotpisan, P., Manasatienkij, W., Nisalak, A., Fernandez, S., Yoon, I.-K., 2015. Detection of Zika virus infection in Thailand, 2012–2014. Am.J.Trop. Med. Hyg. 93, 380–383.

Carver, S., Bestall, A., Jardine, A., Ostfeld, R.S., 2009. Influence of hosts on the ecology of arboviral transmission: potential mechanisms influencing dengue, Murray Valley encephalitis, and Ross River virus in Australia. Vector Borne Zoonotic Dis. 9, 51–64.

Chang, F.-S., Tseng, Y.-T., Hsu, P.-S., Chen, C.-D., Lian, I.-B., Chao, D.-Y., 2015. Re-assess vector indices threshold as an early warning tool for predicting dengue epidemic in a dengue non-endemic country. PLoS Negl. Trop. Dis. 9, e0004043.

Charrel, R.N., Leparc-Goffart, I., Pas, S., de Lamballerie, X., Koopmans, M., Reusken, C., 2016. Background review for diagnostic test development for Zika virus infection. Bull. World Health Organ. 94 (8), 574–584D.

Christofferson, R.C., Mores, C.N., 2015. A role for vector control in dengue vaccine programs. Vaccine 33, 7069–7074.

Diagne, C.T., Diallo, D., Faye, O., Ba, Y., Faye, O., Gaye, A., Dia, I., Weaver, S.C., Sall, A.A., Diallo, M., 2015. Potential of selected Senegalese *Aedes* spp. mosquitoes (Diptera: Culicidae) to transmit Zika virus. BMC Infect. Dis. 15, 492.

Diallo, D., Sall, A.A., Diagne, C.T., Faye, O., Faye, O., Ba, Y., Hanley, K.A., Buenemann, M., Weaver, S.C., Diallo, M., 2014. Zika virus emergence in mosquitoes in southeastern Senegal, 2011. PLoS One 9, e109442.

Eppes, C., Rac, M., Dunn, J., Versalovic, J., Murray, K.O., Suter, M.A., Sanz Cortes, M., Espinoza, J., Seferovic, M.D., Lee, W., Hotez, P., Mastrobattista, J., Clark, S.L., Belfort, M.A., Aagaard, K.M., 2017. Testing for Zika Virus (ZIKV) Infection in Pregnancy: Key Concepts to Deal with an Emerging Epidemic. Am. J. Obstet. Gynecol. pii: S0002-9378(17)30127-8. (Jan 23).

Faye, O., Faye, O., Diallo, D., Diallo, M., Weidmann, M., Sall, A.A., 2013. Quantitative Real-Time PCR Detection of Zika Virus and Evaluation with Field-caught Mosquitoes.

Fine, P., Eames, K., Heymann, D.L., 2011. "Herd immunity": a rough guide. Clin. Infect. Dis. 52, 911–916.

Gasque, P., Couderc, T., Lecuit, M., Roques, P., Ng, L.F., 2015. Chikungunya virus pathogenesis and immunity. Vector Borne Zoonotic Dis. 15, 241–249.

Ginier, M., Neumayr, A., Günther, S., Schmidt-Chanasit, J., Blum, J., 2016. Zika without symptoms in returning travellers: what are the implications? Travel Med. Infect. Dis. 14, 16–20.

Haddow, A.D., Schuh, A.J., Yasuda, C.Y., Kasper, M.R., Heang, V., Huy, R., Guzman, H., Tesh, R.B., Weaver, S.C., 2012. Genetic characterization of Zika virus strains: geographic expansion of the Asian lineage. PLoS Negl. Trop. Dis. 6, e1477.

Hadler, J.L., Patel, D., Nasci, R.S., Petersen, L.R., Hughes, J.M., Bradley, K., Etkind, P., Kan, L., Engel, J., 2015. Assessment of arbovirus surveillance 13 years after introduction of west Nile virus, United States. Emerg. Infect. Dis. 21, 1159.

Hegde, S., Rasgon, J.L., Hughes, G.L., 2015. The microbiome modulates arbovirus transmission in mosquitoes. Curr. Opin. Virol. 15, 97–102.

Higgins, J.P., Green, S., 2008. Cochrane Handbook for Systematic Reviews of Interventions (Wiley Online Library).

Kam, Y.-W., Pok, K.-Y., Eng, K.E., Tan, L.-K., Kaur, S., Lee, W.W., Leo, Y.-S., Ng, L.-C., Ng, L.F., 2015. Sero-prevalence and cross-reactivity of chikungunya virus specific anti-e2ep3 antibodies in arbovirus-infected patients. PLoS Negl. Trop. Dis. 9, e3445.

Kean, J., Rainey, S.M., Mcfarlane, M., Donald, C.L., Schnettler, E., Kohl, A., Pondeville, E., 2015. Fighting arbovirus transmission: natural and engineered control of vector competence in *Aedes* mosquitoes. Insects 6, 236–278.

Kirya, B., Mukwaya, L., Sempala, S., 1977. A yellow fever epizootic in Zika forest, Uganda, during 1972: part 1: virus isolation and sentinel monkeys. Trans. R. Soc. Trop. Med. Hyg. 71, 254–260.

Kleinman, S., 2015. Pathogen inactivation: emerging indications. Curr. Opin. Hematol. 22, 547–553.

Kraemer, M.U., Sinka, M.E., Duda, K.A., Mylne, A., Shearer, F.M., Brady, O.J., Messina, J.P., Barker, C.M., Moore, C.G., Carvalho, R.G., 2015. The global compendium of *Aedes aegypti* and *Ae. albopictus* occurrence. Sci. Data 2.

Kuno, G., Chang, G.-J.J., 2005. Biological transmission of arboviruses: reexamination of and new insights into components, mechanisms, and unique traits as well as their evolutionary trends. Clin. Microbiol. Rev. 18, 608–637.

Kwan, J.L., Kluh, S., Reisen, W.K., 2012. Antecedent avian immunity limits tangential transmission of West Nile virus to humans. PLoS One 7, e34127.

Kwong, J.C., Druce, J.D., Leder, K., 2013. Zika virus infection acquired during brief travel to Indonesia. Am.J.Trop. Med. Hyg. 89, 516–517.

Lanciotti, R.S., Kosoy, O.L., Laven, J.J., Velez, J.O., Lambert, A.J., Johnson, A.J., Stanfield, S.M., Duffy, M.R., 2008. Genetic and serologic properties of Zika virus associated with an epidemic, Yap State, Micronesia, 2007. Emerg. Infect. Dis. 14, 1232–1239.

Laperriere, V., Brugger, K., Rubel, F., 2011. Simulation of the seasonal cycles of bird, equine and human West Nile virus cases. Prev. Vet. Med. 98, 99–110.

Liang, G., Gao, X., Gould, E.A., 2015. Factors responsible for the emergence of arboviruses; strategies, challenges and limitations for their control. Emerg. Microbes Infect. 4, e18.

Mcfarlane, M., Arias-Goeta, C., Martin, E., O'hara, Z., Lulla, A., Mousson, L., Rainey, S.M., Misbah, S., Schnettler, E., Donald, C.L., 2014. Characterization of *Aedes aegypti* innate-immune pathways that limit Chikungunya virus replication. PLoS Negl. Trop. Dis. 8, e2994.

Mcsweegan, E., Weaver, S.C., Lecuit, M., Frieman, M., Morrison, T.E., Hrynkow, S., 2015. The global virus network: challenging chikungunya. Antivir. Res. 120, 147–152.

Medina, G., Garzaro, D.J., Barrios, M., Auguste, A.J., Weaver, S.C., Pujol, F.H., 2015. Genetic diversity of Venezuelan alphaviruses and circulation of a Venezuelan equine encephalitis virus subtype IAB strain during an Interepizootic Period. Am.J.Trop. Med. Hyg. 93, 7–10.

Meister, T., Lussy, H., Bakonyi, T., Šikutová, S., Rudolf, I., Vogl, W., Winkler, H., Frey, H., Hubálek, Z., Nowotny, N., 2008. Serological evidence of continuing high Usutu virus (Flaviviridae) activity and establishment of herd immunity in wild birds in Austria. Vet. Microbiol. 127, 237–248.

Monath, T., Wilson, D., Casals, J., 1973. The 1970 yellow fever epidemic in Okwoga District, Benue Plateau State, Nigeria: 3. Serological responses in persons with and without pre-existing heterologous Group B immunity*. Bull. World Health Organ. 49, 235.

Monath, T.P., Craven, R.B., Muth, D.J., Trautt, C.J., Calisher, C.H., Fitzgerald, S.A., 1980. Limitations of the complement-fixation test for distinguishing naturally acquired from vaccine-induced yellow fever infection in flavivirus-hyperendemic areas. Am.J.Trop. Med. Hyg. 29, 624–634.

Musso, D., Cao-Lormeau, V.M., Gubler, D.J., 2015a. Zika virus: following the path of dengue and chikungunya? Lancet 386, 243–244.

Musso, D., Roche, C., Nhan, T.-X., Robin, E., Teissier, A., Cao-Lormeau, V.-M., 2015b. Detection of Zika virus in saliva. J. Clin. Virol. 68, 53–55.

Musso, D., Roche, C., Robin, E., Nhan, T., Teissier, A., Cao-Lormeau, V.-M., 2015c. Potential sexual transmission of Zika virus. Emerg. Infect. Dis. 21, 359.

Papa, A., Gavana, E., Detsis, M., Terzaki, E., Veneti, L., Pervanidou, D., Georgakopoulou, T., Marangos, M., Koliopoulos, G., Baka, A., 2015. Laboratory and surveillance studies following a suspected dengue case in Greece, 2012. Int. J. Infect. Dis. 30, 150–153.

Pauvolid-Corrêa, A., Juliano, R.S., Campos, Z., Velez, J., Nogueira, R.M.R., Komar, N., 2015. Neutralising antibodies for Mayaro virus in Pantanal, Brazil. Mem. Inst. Oswaldo Cruz 110, 125–133.

Peterhans, E., Zanoni, R., Bertoni, G., 1999. How to succeed as a virus: strategies for dealing with the immune system. Vet. Immunol. Immunopathol. 72, 111–117.

Petersen, E., Wilson, M.E., Touch, S., Mccloskey, B., Mwaba, P., Bates, M., Dar, O., Mattes, F., Kidd, M., Ippolito, G., 2016a. Rapid spread of Zika virus in the Americas-implications for public health preparedness for mass gatherings at the 2016 Brazil Olympic Games. Int. J. Infect. Dis. 44, 11–15.
Petersen, E.E., Staples, J.E., Meaney-Delman, D., Fischer, M., Ellington, S.R., Callaghan, W.M., et al., 2016b. Interin guidelines for pregnant women during a Zika virus outbreak- United States. MMWR Morb. Mortal. Wkly. Rep. 65, 30–33.
Pyke, A.T., Daly, M.T., Cameron, J.N., Moore, P.R., Taylor, C.T., Hewitson, G.R., Humphreys, J.L., Gair, R., 2014. Imported zika virus infection from the Cook Islands into Australia, 2014. PLoS Curr. 6.
Robin, Y., Mouchet, J., 1974. Serological and entomological study on yellow fever in Sierra Leone. Bulletin de la Societe de Pathologie Exotique et de ses Filiales. 68, pp. 249–258.
Rubio, D.M., Schoenbaum, E.E., Lee, L.S., Schteingart, D.E., Marantz, P.R., Anderson, K.E., Platt, L.D., Baez, A., Esposito, K., 2010. Defining translational research: implications for training. Acad. Med. 85, 470.
Salje, H., Lessler, J., Endy, T.P., Curriero, F.C., Gibbons, R.V., Nisalak, A., Nimmannitya, S., Kalayanarooj, S., Jarman, R.G., Thomas, S.J., 2012. Revealing the microscale spatial signature of dengue transmission and immunity in an urban population. Proc. Natl. Acad. Sci. 109, 9535–9538.
Shinohara, K., Kutsuna, S., Takasaki, T., Moi, M.L., Ikeda, M., Kotaki, A., Yamamoto, K., Fujiya, Y., Mawatari, M., Takeshita, N., 2016. Zika fever imported from Thailand to Japan, and diagnosed by PCR in the urines. J. Travel Med. 23, tav011.
Sow, A., Loucoubar, C., Diallo, D., Faye, O., Ndiaye, Y., Senghor, C.S., Dia, A.T., Faye, O., Weaver, S.C., Diallo, M., 2016. Concurrent malaria and arbovirus infections in Kedougou, southeastern Senegal. Malar. J. 15, 1.
Tambo, E., Ugwu, E.C., Ngogang, J.Y., 2014. Need of surveillance response systems to combat Ebola outbreaks and other emerging infectious diseases in African countries. Infect. Dis. Poverty 3, 1–8.
Tambo, E., Chen, J.H., Zhou, X.N., Khater, E.I., 2016 May 27a. Outwitting denguethreat and epidemics resurgence in Asia-Pacific countries: strengthening integrated dengue surveillance, monitoring and response systems. Infect. Dis. Poverty 5 (1), 56.
Tambo, E., Xiao-Nong, Z., 2014. Acquired immunity and asymptomatic reservoir impact on frontline and airport ebola outbreak syndromic surveillance and response. Infect. Dis. Poverty 3, 1–11.
Tambo, E., Chuisseu, P.D., Ngogang, J.Y., Khater, E.I., 2016 May–Junb. Deciphering emerging Zika and dengue viral epidemics: implications for global maternal-child health burden. J. Infect. Public Health 9 (3), 240–250.
Tappe, D., Nachtigall, S., Kapaun, A., Schnitzler, P., Günther, S., Schmidt-Chanasit, J., 2015a. Acute Zika virus infection after travel to Malaysian Borneo, September 2014. Emerg. Infect. Dis. 21, 911.
Tappe, D., Pérez-Girón, J.V., Zammarchi, L., Rissland, J., Ferreira, D.F., Jaenisch, T., Gómez-Medina, S., Günther, S., Bartoloni, A., Muñoz-Fontela, C., 2015b. Cytokine kinetics of Zika virus-infected patients from acute to reconvalescent phase. Med. Microbiol. Immunol. 1–5.
Vazquez-Prokopec, G.M., Kitron, U., Montgomery, B., Horne, P., Ritchie, S.A., 2010. Quantifying the spatial dimension of dengue virus epidemic spread within a tropical urban environment. PLoS Negl. Trop. Dis. 4, e920.
Wauquier, N., Becquart, P., Padilla, C., Baize, S., Leroy, E.M., 2010. Human fatal *Zaire ebola* virus infection is associated with an aberrant innate immunity and with massive lymphocyte apoptosis. PLoS Negl. Trop. Dis. 4, e837.
Weaver, S.C., Forrester, N.L., 2015. Chikungunya: evolutionary history and recent epidemic spread. Antivir. Res. 120, 32–39.
Weaver, S.C., Reisen, W.K., 2010. Present and future arboviral threats. Antivir. Res. 85, 328–345.
Webster, J., Watson, R.T., 2002. Analyzing the Past to Prepare for the Future: Writing a Literature Review. JSTOR.
Yeon-Hee, K., Jae-ku, O., Eun-yong, L., Koung-ki, L., Seong-hee, K., Myoung-heon, L., Se Chang, P., 2015. Seroprevalence of five arboviruses in sentinel cattle as part of nationwide surveillance in South Korea, 2009–2012. J. Vet. Med. Sci. 77, 247.
Zammarchi, L., Stella, G., Mantella, A., Bartolozzi, D., Tappe, D., Günther, S., Oestereich, L., Cadar, D., Muñoz-Fontela, C., Bartoloni, A., 2015a. Zika virus infections imported to Italy: clinical, immunological and virological findings, and public health implications. J. Clin. Virol. 63, 32–35.
Zammarchi, L., Tappe, D., Fortuna, C., Remoli, M., Günther, S., Venturi, G., Bartoloni, A., Schmidt-Chanasit, J., 2015b. Zika virus infection in a traveller returning to Europe from Brazil, March 2015. Euro Surveill 20, 10.2807.
Zink, S.D., Van Slyke, G.A., Palumbo, M.J., Kramer, L.D., Ciota, A.T., 2015. Exposure to West Nile virus increases bacterial diversity and immune gene expression in *Culex pipiens*. Viruses 7, 5619–5631.