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Zika virus infection and its emerging trends in Southeast Asia

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ABSTRACT

Zika virus is a mosquito-borne flavivirus that represents a public health emergency at the ongoing epidemic. Previously, this rare virus was limited to sporadic cases in Africa and Asia until its emergence in Brazil, South America in 2015, where it rapidly spread throughout the world. Recently, a high number of cases were reported in Singapore and other Southeast Asia countries. A combination of factors explains the current Zika virus outbreak although it is highly likely that the changes in the climate and high frequency of travelling contribute to the spread of *Aedes* vector carrying the Zika virus mainly to the tropical climate countries such as the Southeast Asia. The Zika virus is known to cause mild clinical symptoms similar to those of dengue and chikungunya and transmitted by different species of *Aedes* mosquitoes. However, neurological complications such as Guillain-Barré syndrome in adults, and congenital anomalies, including microcephaly in babies born to infected mothers, raised a serious concern. Currently, there is no specific antiviral treatment or vaccine available for Zika virus infection. Therefore, international public health response is primarily focused on preventing infection, particularly in pregnant women, and on providing up-to-date recommendations to reduce the risk of non-vector transmission of Zika virus.

1. Introduction

Zika virus (ZIKV) has become major international health concern in early 2016. ZIKV was primarily known as zoonotic pathogen and can be transmitted by the day-time active *Aedes* sp. mosquitoes. ZIKV was accidentally isolated from a Rhesus monkeys in 1947 during jungle yellow fever research in the Zika forest, Uganda, Africa [1]. The data and findings showed less impact to the society where there were very few articles published as case studies or case reports as only 14 cases were reported since the first documented human infection until 2007 [2,3].

The history of ZIKV in Malaysia dated back to 1969 when the first ZIKV was isolated in *Aedes aegypti* [4]. It is the same vector that transmits Dengue, Chikungunya, West Nile, Yellow Fever and Japanese Encephalitis viruses. Various countries surrounding Malaysia including Thailand, Philippines, Indonesia and Cambodia had reported ZIKV infection among its people but due to its self-limiting and flu-like illness, ZIKV was underreported in Southeast Asia. This tropical region has high prevalence of other arboviral disease which add the burden of the country on its control, surveillance and eventually affecting the management of the disease.

The aim of present review was to highlight the history of ZIKV from its first found and the global spread involved. The main focus was on Southeast Asia due to its high prevalence on arboviral disease. ZIKV has reached to its endemic status in Malaysia followed by Dengue virus.

2. Epidemiology

ZIKV infection in human was first reported in 1952 [5]. It was documented that a 10-year-old Nigerian girl who presented with malarial-like fever with the absence of jaundice, had shown an elevation of specific serum antibodies to ZIKV, which previously happened to be exclusive for monkey species. This discovery prompted further detection of ZIKV infection in human across the African and Southeast Asian countries, including the regions where the day-time mosquitoes are active. However,

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until 2007, the number of confirmed human cases reported, appeared to be low. In these countries, the few occurrences had been regarded as sporadic and the infection had been known to be asymptomatic or it may cause mild symptoms.

The first major outbreak of ZIKV infection documented in 2007 was in Yap Island, where at least 49 confirmed cases with no mortality was reported. Subsequently, in 2013 and 2014, another epidemic was reported in French Polynesia, Easter Island, the Cook Islands and New Caledonia, affecting thousands of people [6]. The massive occurrences of ZIKV infection worldwide has allowed researchers to study extensively on its pathogenesis and possible serious complications (Figure 1). Potentially dangerous complications such as Guillain-Barré syndrome (GBS) and congenital microcephaly that have recently been linked to ZIKV infection have come into the light following the explosive outbreaks in Brazil and Central America since early 2015. The consequent rise in the social and health morbidity associated with ZIKV infection and its complications have urged the World Health Organization (WHO) to announce ZIKV infection as the Public Health Emergency of International Concern (PHEIC) [8]. It is noteworthy that until present, there is no effective treatment and vaccines available for ZIKV infection.

3. Biology of Zika virus

ZIKV belongs to Flaviviridae family. ZIKV is in the form of enveloped and icosahedral measuring about 50 nm in size. ZIKV is closely related to the Spondweni virus and is one of the two viruses in the Spondweni virus clade [9,10]. ZIKV has a non-segmented, single-stranded, positive-sense ribonucleic acid (RNA) genome which is about 10.5–11.0 kbp in size [11,12]. The viral genome produces a polyprotein with more than 3000 amino acids. This polyprotein is then cleaved into three structural and seven non-structural proteins. The flaviviral genome encodes from N- to C-terminal of the polyprotein, the structural C (capsid, w11 kDa), prM (precursor M protein, w26 kDa, which is cleaved into the M protein), and E (envelope, w53 kDa) proteins, and the non-structural NS1 (w46 kDa), NS2A (w22 kDa), NS2B (w14 kDa), NS3 (w70 kDa), NS4A (w16 kDa), NS4B (w27 kDa), and NS5 (w103 kDa) proteins. Structurally, the E and M proteins are located at the surface of ZV. The nucleocapsid is made up of the C protein and the genomic RNA molecule [13].

This RNA genome is directly translated into viral and structural proteins which encapsulate the ZIKV. The replicated RNA strand is held within a nucleocapsid formed from 12-kDa protein blocks. The capsid contains a host-derived membrane modified with two viral glycoproteins. Replication of the viral genome requires creation of an anti-sense nucleotide strand [14]. There are two lineages of the ZV: the African lineage and the Asian lineage (Figure 2). Phylogenetic studies indicate that the ZIKV spreads in the United States of Americas (USA) and French Polynesia belongs to the Asian strain [5,10]. Western hemisphere ZIKV is found to be 89% identical to African genotypes [16].

4. Mode of transmission

ZIKV infection has long been regarded as a vector borne disease. Epidemiologic characteristics of ZIKV transmission are classified into virus vectors, transmission and natural reservoirs. In tropical countries like in Southeast Asia, the mode of transmission most likely occurs via mosquito vectors mainly the *Aedes aegypti* and *Aedes albopictus* mosquitoes. Other strains such as *Aedes africanus*, *Aedes hensilii*, *Aedes polynesiensis*, *Aedes Unilineatus* and *Aedes vittatus* have been identified to be associated with ZIKV transmission in regions with temperate climate [17,18]. The incubation period of ZIKV in this type of mosquitoes is about ten days [19,20]. In *Aedes aegypti*, high viral load is found between 20 and 60 days following infection [21].

The most recent large scale epidemic of ZIKV infection in Brazil in 2015 prompted advanced knowledge albeit inconclusive on the modes of its transmission. For instance, parenteral, sexual and perinatal routes of transmission are possible. Musso *et al.* [22] demonstrated the possible ZIKV transmission by blood transfusion during an outbreak in French Polynesia as evidenced by positivity of ZIKV in the blood donor by reverse transcription polymerase chain reaction (RT-PCR) and viral culture study.

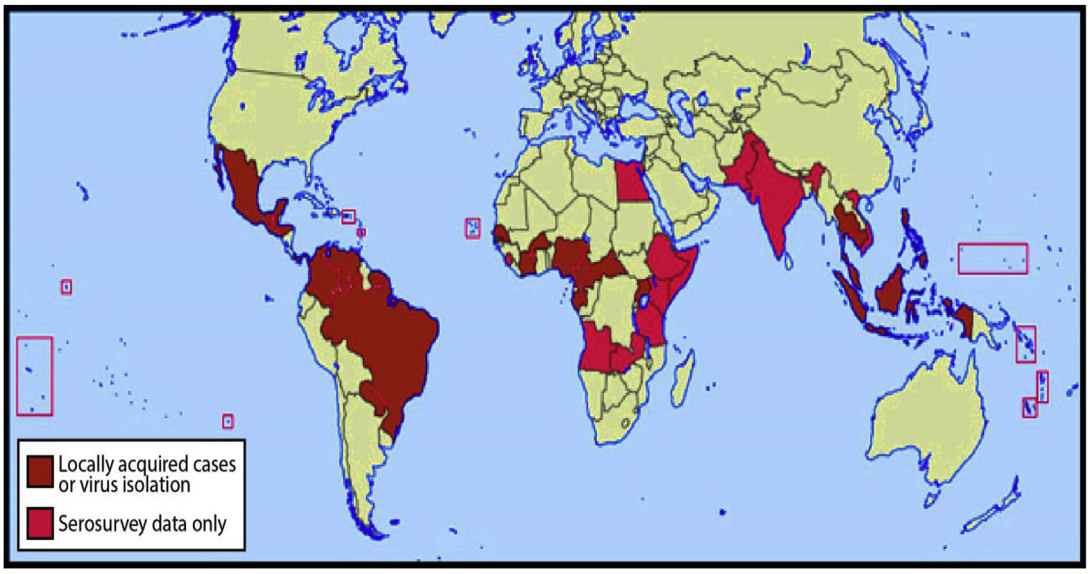

Figure 1. Countries with past or current evidence of Zika virus transmission (as of December 2015) [7].

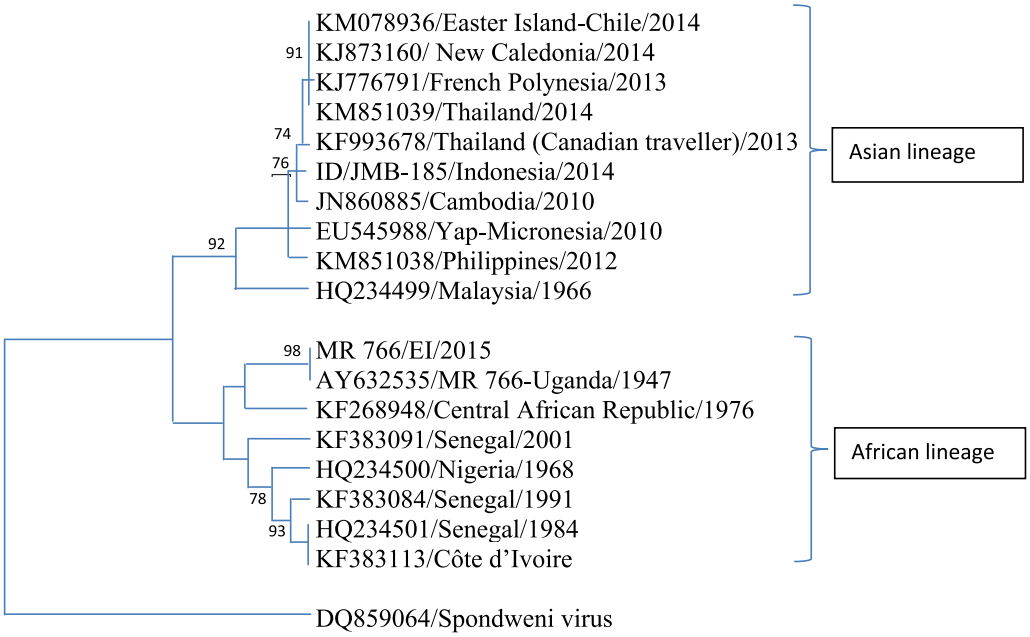

Figure 2. Phylogenetic tree exhibits two main lineages of Zika virus [15].

Although the parenteral transmission through blood transfusion remains a subject of research, it is suggested that the risk of transmission is possible as there are reports of transmission of the related viruses (Dengue, Chikungunya and West Nile viruses) by blood transfusion. Recently, it was reported that ZIKV can be transmitted via anal and vaginal sex. Both male–male and male–female transmissions are possible. The common feature observed in the sexual transmission of the ZIKV is that the infected individual had a history of travelling to the epidemic areas of ZIKV infection. The infection is transmitted to the partners a few days before or after the onset of the symptoms [23]. Clinically prostatitis, haematospermia and serological finding confer to the impression that ZIKV replication may take place in the genitourinary tract, in which the testes or prostate can serve as the reservoirs. It has been documented that ZIKV is present in the semen after more than two months of disappearance of the symptoms [24–26]. In vertical transmission, the risk of ZIKV infection from mother to foetus has gained a growing concern among the population. Based on the observational data in Brazil, the occurrence of microcephaly may be related to the possibility of ZIKV to pass through the placenta and injure the developing neurons, including that constituting the brain [6,8].

5. Clinical features

In this review, we collected data of clinical presentations of ZIKV infection, with a total of 134 cases reported in 32 case reports, since 1964 till 2016 [3,17,18]. For each sign and symptom, frequency of its presentation reported in each case was cumulated and presented as percentage (Figure 3).

The most common symptom presented in ZIKV infection is rash, in which it is present in 82.1% of the reported cases [3,17,24]. The first documented human ZIKV infection reported the rash as maculopapular covering the face, trunk and upper arms [19,27]. Similar presentation was reported in two travellers in Japan and

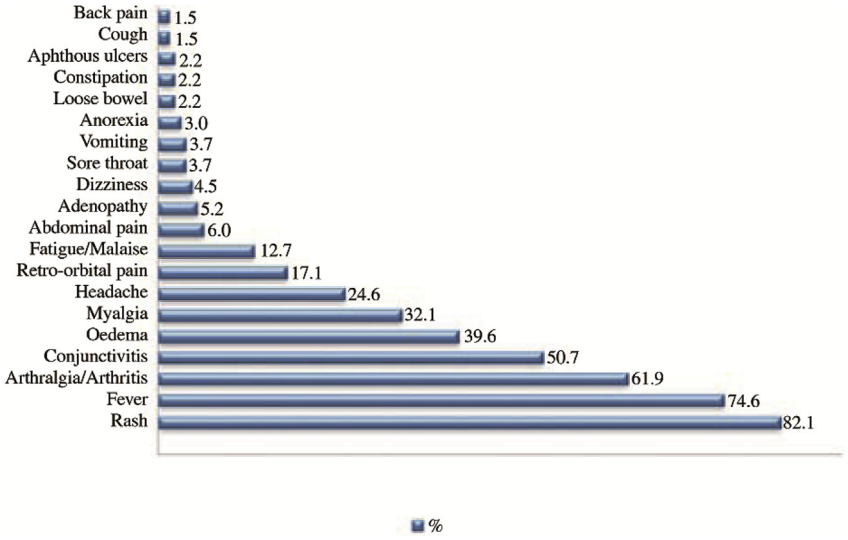

Figure 3. Percentage of signs and symptoms of Zika virus infection presented in 134 cases which are reported in 32 case reports. For each sign and symptom, frequency of its presentation reported in each case was cumulated and presented as percentage.

one traveller in Swiss [28,29]. Foy *et al.* [24] reported three cases which developed maculopapular rash involving only the torso.

ZIKV infection is sometimes referred to as Zika fever [28,30]. However, about 25.4% of reported cases of ZIKV infection did not develop fever [24,31,32]. Compared to other arborvirus infections particularly Dengue and Chikungunya, ZIKV infection most commonly presents as mild fever, even though in some cases it may reach up to 39 °C [33].

The third most common symptom of ZIKV infection is arthralgia, which was present in 61.9% of reported cases [24,25,34]. Arthralgia commonly involves peripheral small joints such as the wrist, hand, ankle and foot [24,35,36]. However, in some cases it involves bigger joint such as elbow and knee [24,29]. It is commonly associated with oedema which was present in 39.6% of reported cases [24,29,35,36]. Myalgia and back pain were reported to be present in 32.1% and 1.5% of the cases [3,18,24].

Conjunctivitis were present in 50.7% of cases, which is the fourth commonly reported symptoms and mostly involved both eyes [34,37,38]. Headache, retro-orbital pain and dizziness were present in 24.6%, 17.1% and 4.5% of reported cases respectively [27,39,40].

ZIKV symptoms may also presented with gastrointestinal symptoms for example abdominal pain 6.0%, vomiting 3.7%, loose bowel 2.2% and constipation 2.2% [3,18,33,41]. It may also associate with constitutional symptoms, fatigue was presented in 12.7% and anorexia presented in 3% of reported cases [31,42,43]. In small amount of patients, it may present with sore throat, 3.7% and cough, 1.5%, which may mimic upper respiratory tract infection [17,18,36,44]. Other symptoms that are associated with ZIKV infection are adenopathy and aphthous ulcers which are present in 5.2% and 2.2% of cases [29,41,42].

ZIKV infection may associate with neurological manifestation. Cao-Larmeau *et al.* [34] reported 42 cases of GBS had encounter with ZIKV infection, with 100% had neutralising antibodies against ZIKV and 98% of patients had anti-ZIKV IgM or IgG, in which neurological symptoms developed within six days of ZIKV infection. Mecharles *et al.* [45] reported a case of acute myelitis, in which the patient presented with left hemiparesis associate with paresthesia, developed seven days following ZIKV infection. Carteaux *et al.* [46] reported a case of ZIKV infection associated with meningoencephalitis, in which patient presented with left hemiplegia and right upper limb paresis. ZIKV infection is also associated with hearing difficulties in which the patient had sudden bilateral metallic and dull sound, and experienced a short delay between a sound and the perception of sound [36].

ZIKV infection had been reported to involve urinary and reproductive organs. Foy *et al.* [24] reported prostatitis developed associated with ZIKV infection, in which patient presented with perineal pain and dysuria that is associated with haematospermia. Another case of haematospermia was reported by Musso *et al.* [25]. Atkinson *et al.* [26] reported positive RT-PCR in semen which may suggest possibility of sexual transmitted disease. Olson *et al.* [41] reported haematuria developed associated with ZIKV infection. Gourinat *et al.* [37] suggested urine is preferable compare to serum in detection of ZIKV because ZIKV presence for a longer duration and higher titres in urine.

There were possibility of association of bleeding in ZIKV infection, even though less when compare to Dengue and Chikungunya, in which gingival bleeding, haematuria and haematospermia had been reported to be associated with ZIKV infection [24,25,41,42].

Arzuza-Ortega *et al.* [33] reported mortality in a 15-year-old girl with underlying sickle cell disease that had an encounter with ZIKV infection. The patient presented with high grade fever, arthralgia, myalgia, retro-ocular pain, abdominal pain and jaundice. Physical examination revealed generalized jaundice, severe abdominal pain, hepatosplenomegaly, tachycardia, holosystolic murmur, respiratory distress with Glasgow Coma Scale (GCS) score of 13. Despite on mechanical ventilator support, patient succumbed after 37 h. This suggest that patients with underlying sickle cell disorders presented with suspected arboviral infections should be recommended to be under close monitoring.

Besnard *et al.* [47] reported two cases of ZIKV infection in newborn, with one of the newborn developed rash following breast feeding. ZIKV particles had been reported to be present in breast milk by cytopathic effect and by quantitative reverse transcription PCR (RT-qPCR) [48]. Hydrops foetalis, microcephaly and other foetal brain abnormalities had been reported to be associated with ZIKV infection suggesting possibility of perinatal transmission [31,40,49].

6. Countries affected by Zika virus

6.1. Worldwide

It is a mandatory to have worldwide surveillance in the ZIKV affected areas due to the prompt geographical expansion of ZIKV transmission and its complication including microcephaly and congenital abnormalities. ZIKV infection alarmed the world with initial detection in Brazil in 2015–2016 [50–53]. However, according to the reports, ZIKV was introduced in USA in the year 2008, and at least a year before in Micronesia in 2007. A brief summary of the worldwide affected area, the detection period and the findings were mentioned in Table 1.

6.2. Zika virus in Southeast Asia

Earlier reports showed that the number of ZIKV studies in Southeast Asia is relatively low compared to the other regions in the world. In Southeast Asia, ZIKV was first identified in the 1960s. ZIKV infection cases in human was believed to be underreported mostly attributed to the confusion with Dengue virus infection and difficulty in gaining laboratory confirmation [15,61]. It is well understood that the allocation for research in the developing or low to middle-income countries is being prioritised for the current major issues, hence, the investigations on ZIKV infection cases have been side-lined due to mild and sporadic cases.

ZIKV was believed to disseminate in the Southeast Asia in the last 50 years or so [16]. Typically, the tropical Southeast Asian countries are more likely to be burdened by ZIKV infection as compared to the non-tropical countries due to its distinguished climate that is favourable for the rapid breeding of the potential vectors. ZIKV infection poses a great challenge to the tropical Southeast Asian countries primarily due to the uncontrolled thrives of *Aedes* genus mosquitoes. Furthermore, increasing prevalence of ZIKV infection in Southeast Asian countries is considered challenging due to the expansion of the tropical belt and the global warming effect.

Table 1
A brief summary of worldwide Zika virus infection affected area with the findings.

Country	Period of study	Type of study	Detection methods	Findings	Refs
Brazil	April 2015–January 2016	Review of case reports	RT-qPCR	Early introduction and presence (mid-2014) of ZIKV in the Salvador region in Bahia, Brazil.	[50]
Brazil	January–May 2016	Review of case reports	1. Central nervous system (CNS) abnormalities detected by cranial computed tomography (CT) scan, with or without microcephaly; and 2. Negative results for syphilis, toxoplasmosis, rubella, cytomegalovirus, and herpes (STORCH) on serologic tests of the infant after delivery.	Early growth and neurologic outcomes of infants with probable congenital ZIKV syndrome in the first 8 months of age.	[51]
Italy	2016	Case reports	Real-time reverse transcription PCR (rRT-PCR) of ZIKV RNA of serum, urine, saliva and vaginal swab	ZIKV RNA was detected in serum (day 6), urine (up to day 27), cerebrospinal fluid (day 6), saliva (up to day 13), and vaginal swab (up to day 13). ZIKV-specific antibodies in serum were confirmed by microneutralization assay.	[54]
New Zealand	2016	Case reports	rRT-PCR in semen	It occurs via sexual transmission and the ZIKV RNA persists in semen.	[55]
Panama	2016	Case reports	RT-qPCR of serum and urine	1. Most commonly reported signs and symptoms were fever (86%), exanthema (72%), and headache (62%). 2. Ultrasound monitoring pregnant mothers with serological positive ZIKV provide relatively low positive predictive value for detecting microcephaly.	[56]
Portugal	2008–2016	Descriptive study	Analysis of temporal patterns according to classification of admissions: 1. Congenital malformations of the nervous system (International Classification of Diseases, 10th Revision [ICD-10] Q00-Q07) in children <1 year of age; 2. GBS (ICD-10 G610); 3. Other potential and unspecific clinical manifestations such as encephalitis, myelitis, and encephalomyelitis (ICD-10 G040-G049); 4. Abortion and related problems (ICD-10 O03-O07); in particular; 5. Spontaneous abortion (ICD-10 O03)	Increases in the number of hospitalizations for congenital malformations of the nervous system, GBS, and some inflammatory diseases of the CNS.	[57]
Guatemala & Puerto Rico	December 2015	Case reports	RT-qPCR of serum	Transcontinental movement of ZIKV-The percent nucleotide identity among all the Western Hemisphere ZIKV is >99%, and as a group, these Western Hemisphere viruses are ≈89% identical (96% aa) to viruses of the East African and West African genotypes.	[58]
Colombia	October–November 2015	Case reports	RT-qPCR	ZIKV circulating in Colombia could have been imported from Brazil, most likely as a result of tourism activities on Colombia's northern coast	[59]
Colombia	October 2015	Case reports	RT-qPCR	Patients with sickle cell disorders and suspected arboviral infections should be closely monitored.	[33]

(*continued on next page*)

Table 1 (*continued*)

Country	Period of study	Type of study	Detection methods	Findings	Refs
Brazil	April–June 2015	Case reports	rRT-PCR	Signs or symptoms of ZIKV are headache (67%), fever (67%), arthralgias (58%), myalgias (49%), and joint swelling (23%). Conjunctivitis was observed in 39% case-patients and retro-orbital eye pain was reported by 40%.	[52]
Brazil	April 2015	Case reports	CT scans and magnetic resonance imaging (MRI) to assess microcephaly	Although studies showed initial lacked ZIKV testing and completed only partial testing for TORCHES infections, the timing on the microcephaly and the history of rash in more than half of the pregnant mothers suggest an outbreak of congenital microcephaly caused by a congenital infection	[53]
New Caledonia	2014	Case reports	RT-qPCR	Awareness of infections with multiple pathogens in the differential diagnosis of Dengue-like illness, especially in patients who returned from tropical regions.	[48]
French Polynesia	2013	Case reports	RT-qPCR	Sequencing of 1 ZIKV-positive sample from a patient in Nuku Hiva, Marquesas Islands (GenBank accession no. KJ579442) showed that it had 100% homology with the fragment sequenced from patient 4 who lived in Tahiti, Society Islands.	[34]
United States of America	2008	Case reports	RT-qPCR	Patients were infected with ZIKV, probably in Southeastern Senegal, by bites from infected mosquitoes	[24]
Micronesia	2007	Case reports analysis	IgG ELISA, RT-qPCR & Nucleic Acid Sequencing and Phylogenetic Analysis		[60]

Apart from Brazil, the focus on ZIKV now is on the Southeast Asia countries. This was due to the occasions where a few of the travellers especially from USA or European countries got infected with ZIKV following a short trip or travelling to Southeast Asia countries. Generally, the infected individuals were diagnosed only when there were already in their hometown. Center for Diseases Control and Prevention (CDC) has prepared guidelines and precautions especially for those individuals who want to travel or have a short trip to Southeast Asian countries.

In recent years, multiple sporadic cases were reported in Cambodia, Philippines, Thailand, Singapore and Malaysia. Most of the reported cases were local infection. However, there were some cases reported which were imported cases involving travellers [17,18].

In 2010, a 3-year-old boy was confirmed to have ZIKV infection through RT-PCR after he presented with four days history of fever and upper respiratory tract infections. However, serological investigation on Dengue and Chikungunya infection were negative. The boy was not hospitalised and follow up interview reported that the boy had fully recovered from the infection [44].

Two years later, a 15-year-old boy in Cebu City, Philippines, presented with fever and other symptoms which include headache, conjunctivitis, sore throat, myalgia, stomach pain, anorexia, nausea, vomiting but no rash. Otherwise, he had no recent travel history and no other family members of his household were ill. The boy recovered fully and did not require hospitalisation. ZIKV infection in this case was confirmed by RT-PCR and genetic analysis [18].

In the same year, a case of ZIKV infection was reported in a 52-year-old healthy Australian woman who returned from Indonesia with fever and rash. She presented with malaise, rash and mild conjunctivitis after a nine days holiday to Jakarta, Indonesia. At first, provisional diagnosis was Dengue fever as evidenced by the positive dengue serologic analysis and generic flavivirus group PCR. However, sequencing of the original flavivirus PCR product identified it as ZIKV (GenBank accession no. KF258813) [39].

From the year 2012 until 2014, seven cases of acute ZIKV infection were reported in Thai residents across the country confirmed by molecular or serological testing including sequence data. These cases were considered local infection in the Thais. Their clinical presentation was mild and non-specific which include fever, maculopapular rash, arthralgia, myalgia, headache, sore throat and rhinorrhoea. Only two patients complained of conjunctivitis. In May 2013, the Thai Ministry of Public Health was notified that ZIKV infection had been confirmed in a Canadian traveller to Thailand [17].

In 2016, Singapore announced its first ZIKV infection in May, with the virus imported by a 48-year-old man who had travelled to Brazil. However, the recent outbreak of ZIKV infection was not linked to the imported strain since it has been found that the virus belongs to the Asian lineage and likely evolved from the strain that was already circulating in Southeast Asia. The Ministry of Health and National Environment Agency have been informed of the first locally-transmitted ZIKV infection in August 2016. The patient is a 47-year-old female Malaysian who resides at Block 102 Aljunied Crescent and works in Singapore. As she had no prior recent history of travelling to Zika-affected areas and she was likely to have been infected in Singapore. The patient had developed fever, rash and conjunctivitis from 25 August. She visited a general practitioner on 26 August and was referred immediately to Communicable Disease Centre of Tan Tock Seng Hospital and was tested positive for ZIKV the next day. She was hospitalised for observation and fully recovered [62].

Since the first case reported, Singapore has been put on high alert for transmission of ZIKV infection taking into account for the presence of ZIKV in the region and the volume of travel by Singaporeans and tourists. Sources compiled by Communicable Diseases Division, Ministry of Health Singapore stated that cumulative number of cases for 2016 since the first case until early November showed approximately 446 cases.

In September 2014, acute ZIKV infection was reported in Germany after travelling to East Malaysia (Borneo). In outpatient clinic in Germany, 45-year-old woman presented with fever, exanthematic arthralgia syndrome and sudden bilateral hearing difficulties on the day 7 following her trip from Malaysia. She was confirmed to have ZIKV infection following a serological investigation [36].

Malaysia has reported its first case of ZIKV infection in August 2016. A 58-year-old woman from Klang, Malaysia, had shown clinical presentation of fever and rash after one week returned from Singapore. She was confirmed to have ZIKV infection by laboratory investigation, blood and urine sample. Her daughter, who lives in Singapore, was also infected [63].

The second case was reported in September and it was a local infection in East Malaysia, Sabah. A 61-year-old man, with underlying multiple co-morbidities, presented with worsening fever, muscle aches and diarrhoea. He was confirmed of ZIKV infection by blood and urine samples. Unfortunately, the patient passed away from complications caused by his underlying heart disease. Government official from the Ministry of Health Malaysia said that the death of the patient is due to the underlying co-morbidities where the patient had suffered before since he only experienced mild clinical features of ZIKV infection [64].

The third case reported was in the same month, which was confirmed as the first case of pregnant woman infected with ZIKV. A 27-year-old woman from Johor Bahru, Malaysia, a primigravida, around 13 weeks period of amenorrhoea (POA), presented with fever and exanthematic arthralgia syndrome. Her husband also experienced the similar symptoms. Both was confirmed to have ZIKV infection by serological investigation and had history of travelling to Singapore six months ago. In addition, her husband had been travelling between Malaysia and Singapore daily for his job in Geylang (an area close to a Zika cluster named by the Singapore authorities) [65].

While the symptoms are treatable, vaccines are not yet available to prevent and contain ZIKV infection from spread. Integrated control measures consisting the public awareness and education and reduction in the vector mass are being undertaken by the Southeast Asia countries. Although the majority of the cases appeared to be mild and the complications of ZIKV infection are relatively rare, precautions and control measures need to be undertaken to limit the spread of infection. As the emergence of the major outbreak of ZIKV and its complications in 2015, it is likely that Southeast Asia countries will be more active in the prevention, diagnostic evaluation and research output related to ZIKV infection.

7. Conclusions

In conclusion, the accumulative evidences showed that ZIKV infection is a major public health emergency for Southeast Asian countries. ZIKV is most likely spread from the travellers' as Southeast Asian countries are well-known for its tourist attractions. Proper screening with guideline, monitoring and precaution measures should be implemented to all the travellers entering into the Southeast Asian Countries. Moreover, domestic awareness and public health campaign are needed to implant in these countries. Future studies with multidisciplinary effort are essential to provide the better diagnostics and therapeutics effects.

Conflict of interest statement

We declare that we have no conflict of interest.

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