Zika virus: fourth pandemic threat of the last decade

Zika virüs: son on yılın dördüncü pandemi tehdidi

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Abstract

After its first discovery for 70 years, World Health Organization has classified the Zika virus (ZIKV) as a global health risk. The ZIKV that is transmitted to human by some species of Aedes mosqui tos has caused sporadic and epidemic infections generally in tropical and subtropical regions to date. Though it mainly produces a self-limiting febrile rash disease in symptomatic cases, its real significance has been better understood after detection of its ability to promote immune-mediated neurologic disorders such as Guillain Barre syndrome in healthy adults following the acute infection, and microcephalia in the fetus of infected pregnant women. In addition to vectors, its ability to spread by bloodborne and sexual route were recognized as the most potent feature of ZIKV to spread in population. Wide global distribution of the vectors, including our country, poses a substantial continuous risk for Turkey. Furthermore, increasing human movement due to the Olympic Games that will be held in Brazil in 2016 summer, where the virus is the most prevalent country, is a growing concern about augmenting the spread of virus to the world. In this review, latest data about the ZIKV transmission, health problems caused by, and treatment properties were aimed to be evaluated in a historical progress, and some preventive measurements were suggested.

Keywords: Zika Virus; Pandemic; Flaviviridae.

Zika virus (ZIKV) is an enveloped, single-chain, positive-polarity RNA virus from the Flaviviridae family. This family also consists of Dengue virus, West Nile virus, Japanese Encephalitis virus, Yellow Fever virus and Tickborne Encephalitis virus, and these pathogens share such common features including arthropod-borne transmission, fever, skin rashes, and neuronal invasion (1). The virion structure of Zika virus is shown in Figure 1.
where ZIKV is seen most often (3). The World Health Organization (WHO) has therefore conducted the fourth pandemic induction for ZIKV, after past 10 years (4).

Our country is a risky geographical area for Zika virus. Therefore, it is important for health workers, national health authorities and citizens have sufficient knowledge about this virus. In this review, it is aimed to provide information about the health workers, health administrators and citizens, and suggestions about the measures that can be taken by evaluating the current literature about ZIKV.

Scientific studies published by April 15, 2016 on Zika virus have been reviewed. For this purpose, PubMed, Web of Science, Google Scholar and Inonu University Library electronic databases were used and a total of 395 publications were evaluated. Of these, 48 studies (36 full texts and 12 abstracts) were used in the scope of this review.

Three major epidemics that caused by the agent in the historical process of recognition of Zika virus were examined; the route of transmission of the agent, the clinical conditions caused by it, and the data obtained on preventive and therapeutic interventions were summarized, and evaluated in this study.

Zika Virus Recognition Processes and Epidemics

Zika virus was first detected by Dick et al. in 1947, in a Rhesus monkey with high fever during a yellow fever survey in the Zika forest near Uganda’s Victoria watershed; and one year later, some mosquitoes in the region were found to be infected with virus (5,6). About seven years later, an epidemic jaundice study in Nigeria reported the first human infection caused by ZIKV in three patients (7). In Kenya, the border region of Uganda and the eastern shores of Lake Victoria, a national survey lasted from 1959 to 1960, surveillance of arbovirus seropositivity in about 3000 people from different parts of the country and more than half of the people living along the coast of the Indian Ocean found ZIKV antibodies (8). In the following years, studies on seroprevalence of ZIKV continued to be produced and ZIKV seropositivity was also found in different countries of Africa (9, 10). On the other hand, from the late 1960s, a report on Zika virus infections was issued from Malaysia (11), which was regarded as the first indication of the virus spreading out of the African continent. Virus were also detected in serum samples from seven patients who had not been enrolled in Indonesia for 1,900 years, and in 1983, more than 2% of the samples taken in Pakistan were found to have ZIKV seropositivity (12, 13).

1. Yap State Epidemic

Up to 2007, the number of acute patients described in the literature was around 10, while the first ZIKV epidemic was reported in Yap State, an island of Micronesia from Oceania, infecting about 70% of the island’s inhabitants and suffering from fever and rash. In the in progresses of the genome sequence; it was found that the epidemic virus was similar to the first species in Uganda in 1947 by 88.9% at the nucleotide level and 96.5% at the amino acid level (14). In the ongoing studies of this epidemic; no mosquito-type epidemic virus has been shown to be present, although the region has been predominantly a clone of *Aedes serratus* mosquitoes (15).

By the time of 2008, about two weeks after returning to the United States, scientists in Senegal showed symptoms of the disease and three days later similar symptoms of infection were seen in the spouse of one of them (16). It is thought that the infection developed in this third person, who has never traveled to the area where the disease has been seen, is infected with the vector-independently of its partner. This study has gained importance in that it shows the first infection report outside the tropical and subtropical regions and that the virus can be transmitted without vectors. Meanwhile, reports have been made that the virus is beginning to appear in Australia (17).

2. Polynesia Outbreak

Towards the end of 2013, a major epidemic emerged from the French Polynesia, an island community in the Pacific Ocean, where fever, rash, joint pain and conjunctivitis were observed. More than 6,000 patients were found to be infected with this virus, none of the patients were required to be admitted to the hospital, and more than 75% of patients were shown positive by molecular methods (18). When returning to two Japanese tourists to their countries traveling to the outbreak area, they showed similar disease symptoms and thus reached Japan from the ZIKV epidemic area (19). An epidemic of this magnitude has attracted the attention of world medical authorities and is thought to be evidence of how highly contagious the virus can be in appropriate conditions. However, the fact that ZIKV was able to form a mild clinical picture that improved spontaneously led to its limitation being limited. This continued until the footsteps that had left the epidemic in the following months pointed to serious health problems. In a case reported in March 2014, a 40-year-old female patient afflicted with an epidemic was
admitted to the hospital with a diagnosis of Guillain-Barré syndrome due to a progressive neurological deficit, and the clinical condition was associated with ZIKV infection about one week earlier (20). Molecular analysis of disease symptoms in infants born to two mothers affected by the epidemic showed that ZIKV could be transmitted to the baby via transplacental or vertical pathway by showing virus RNA in the blood of newborns (21). This was followed by studies that Musso and colleagues reported were able to cross the blood transfusions with the agent. Researchers showed viral RNA in 42 out of 1505 blood donors (3%) in the study they performed in the outbreak area (22). More extensive studies after this outbreak in Polynesia have reported that the affected population is actually about 28,000 people, ZIKV infection is detected in almost all post-epidemic islands and that the incidence of Guillain-Barré syndrome in the epidemic area has increased by about 20 times in the following episodes (23).

The occurrence of Zika virus in European countries has often been attributed to the fact that travel to the region has been influential. A German tourist who returned from a trip to Thailand at the end of 2013, the disease started with symptoms of arthritis and arthralgia in the knee and toe joint and was serologically defined as the first case of ZIKV in Europe (24). Two Italian tourists returning from French Polynesia later showed the similar symptoms, and the virus was confirmed later (25).

In the following months, ZIKV has also been found to be present in urine and saliva, and it is predicted that other such body fluids may also play a role in the spread of the agent (26, 27).

3. Brazil Epidemic
In June 2015, ZIKV RNA was detected in people who had Zika virus infection-like symptoms in the northeastern region of Brazil where Dengue virus was endemic, and this was the first report to indicate that the agent was in Brazil (28). In this study, the authors did not provide data on how the disease reached the region, and thought that the environmental conditions were indigenous to other arbovirus spreads. After this epidemic, Latin American countries were identified as high risk areas for ZIKV due to the endemic presence of vector mosquito species (29). However, in subsequent studies it was reported that the virus was genetically originated from the Polynesian epidemic (genomic similarity 99.9%), possibly in Brazil, and may have moved to the country during the 2014 World Canoe Racing teams of the Oceania islands where French Polynesia and some other viruses are endemic (30, 31). However, Northeast Brazil is geographically very close to the African continent where ZIKV was first identified and endemic. Nevertheless, the virus has provided important information about the entry of the virus into the country from the Pacific Ocean over about twice the distance, demonstrating that the agent is carried by more human movements, and illuminating the virus transmission dynamics. The endemic virus in Brazil is rapidly spreading and has caused disease development in some 15,000 people within a few months (32). By November 2015, WHO reported that ZIKV was endemic in 18 out of 27 Brazilian states (33); the virus was also found in other South American countries such as Venezuela (34) and in some states of North America in the United States (35). While the virus is spreading to Brazil, the data about the factor have increased even more; it has been reported that microcephaly and ocular complications develop in infants of mothers who are infected during pregnancy (36, 37). Detailed investigations have shown that infants born to affected mothers develop eye complications such as intense pigmentation and macular changes such as chorio-retinal atrophy and hypoplastic optic nerve development (38). In a later reported case, a 39-year-old adult with active infection developed hypertensive iridocyclitis in one eye (39). This phenomenon is considered to be the second most important complication detected in adults.

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Clinical Findings
The obtained data show that symptoms of disease occur in every 5 individuals who are infected with Zika virus (42). General clinical findings detected in patients; mild fever, moderate conjunctivitis, muscle and joint pain, and maculopapular rash. However, it has been reported that depending on the characteristics of the individual, these symptoms may be more severe, and in some cases other health problems, especially the nervous system, may also be seen. In surveillance surveys, ZIKV exposure in early pregnancy (first trimester) was found to be the most important risk factor in the development of neurological complications. (43). In another surveillance case, eye problems were found in 10 (35%) of 29-year-old infants who had ZIKV infection in the first trimester (44). The clinical symptoms and complications caused by the etiology group are shown in Table 1.
Table 1. Clinical Symptoms of ZIKV infection.

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Features</th>
<th>Character</th>
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</thead>
<tbody>
<tr>
<td>Healthy Adults</td>
<td>Fever</td>
<td>37-39°C</td>
</tr>
<tr>
<td></td>
<td>Conjunctivitis</td>
<td>Mild-moderate</td>
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<tr>
<td></td>
<td>Fatigue</td>
<td>Widespread</td>
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<tr>
<td></td>
<td>Arthralgia</td>
<td>On abdomen and extremities</td>
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<tr>
<td></td>
<td>Maculopapulillary skin rashes</td>
<td>Generalized, postauricular</td>
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<tr>
<td></td>
<td>Lymphadenopathy</td>
<td>Hypertansif, unilateral</td>
</tr>
<tr>
<td></td>
<td>Iridocyclitis</td>
<td>Acute motor axonal neuropathy</td>
</tr>
<tr>
<td>Fetus</td>
<td>Microcephaly</td>
<td>Periventricular calcification, reduced gyrus curves</td>
</tr>
<tr>
<td></td>
<td>Ocular complications</td>
<td>Macular pigmentation</td>
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<td></td>
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<td>Loss of foveal reflex</td>
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<td>Atrophy in ophtalmic nerve</td>
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<td></td>
<td></td>
<td>Corio-retinal scar</td>
</tr>
<tr>
<td></td>
<td>Maculopapulillary skin rashes</td>
<td>On abdomen and extremities</td>
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DISCUSSION

Zika virus has now become widespread in endemic situations in tropical and subtropical Africa, southern and southeastern Asia, Oceania and Latin America (45). In North American and European countries, sporadic infections related to travel to endemic areas are still found. ZIKV infection has not yet been reported in our country. Zika virus; causing a self-limiting, acute and rash infection pattern. However, the main concern in this regard is serious neurological complications. Besides virus, vector mediated transmission, blood circulation and transmission by sexual intercourse also pose a significant risk for community health.

The fact that the agent is also present in the saliva, urine and tear fluid increases the anxiety that it may spread more rapidly. These properties are a major problem for the spread of ZIKV in geographical regions where vectors have few or absent.

Some potential risks associated with Zika virus transmission in the data obtained from investigations are predicted by us: I. The human population all over the world is at risk for ZIKV infection as the vector can carry out vector mediated transmission. However, if there are no biological reservoirs of the virus in the geographical region where infections are to be formed in this way, the potential for resuming after the epidemic is low. On the other hand, it is more appropriate to be suspicious of this situation because the availability of the agent is not fully known in local mosquitoes living in areas where the agent has not yet arrived. Moreover, in mammals living in such areas, the potential for making ZIKV illness and reserve is uncertain.

II. Since it can be found in many body fluids other than viruses, blood and genital extracts, it can be seen that in societies with low socio-economic level and in hygienic conditions, the potential for domestic diffusion is high. It can be predicted that these epidemics in Brazil and other South American countries, which are progressing rapidly and intensely, have strengthened the epidemic with domestic spread as well as the possibility that all cases have only been infected with mosquitoes. At this point, Turkey has similar spread risk in many developing countries. Ill. Having reserves in the viral vectors constitutes the potential for its endemic spread. In this respect, the Thrace region of our country is particularly at risk because it contains Aedes albopictis species vectors, although not very common (47). IV. There is no data on the transmission of virus through the respiratory tract and food. It may be useful to take the necessary precautions to prevent such potential contamination until the data are available. V. The virus has a high potential for spread in public places such as hospitals, schools, prisons and military camps. Especially in these areas, it is appropriate to take precautions, increase vector control and hygienic conditions.

An effective antiviral drug that can be used in Zika virus infections has not yet been identified. With the initiation of vaccine trials, an effective vaccine has not yet been produced (46). Therefore, women in endemic areas should not be pregnant, postponing trips to endemic areas, fighting with vectors and increasing hygienic conditions are the main measures against ZIKV (48).

There are still a lot of unknowns about Zika virus. In the coming months, when mosquitoes will be active in the near future, there is a risk that human mobility due to sports activities in Brazil will carry the virus to the whole human population. It is crucial for the state to analyze the risks of these epidemics, to determine priorities, to formulate an action plan, to inform the public and to prepare health institutions for this issue.
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