



## Case report

## Zika virus infection in a newly married Greek couple



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## ABSTRACT

Zika virus (ZIKV) is a member of the *Flaviviridae* family causing asymptomatic or mildly symptomatic infections with fever, rash, arthralgia and headache. It is transmitted by the *Aedes* species mosquitoes and also sexually and transplacentally, and has been recently associated with congenital neurologic birth defects in South and Central America. We report the case of a newly married couple from Greece who travelled to Cuba for their honeymoon and developed mild symptoms consistent with arboviral infection. After returning to Greece, they were found to have been infected by Zika virus during their honeymoon. These are the first two cases of Zika virus infection in Greece, the southeastern border of Europe, denoting that Zika virus infection poses a threat for public health worldwide, since returning travelers could be asymptomatic carriers of the virus, not only leading to risk of neurologic birth defects for their offspring but also the real risk of transmission of the virus in their country by local *Aedes* mosquitoes.

## Introduction

Zika virus (ZIKV) is a member of the *Flaviviridae* family, and was initially isolated in Uganda in 1947 [1]. Along with the other members of that family, infection by ZIKV is usually asymptomatic, but when symptoms develop, they are usually minor such as fever, rash, arthralgia and headache, making the differentiation from other tropical mosquito-borne diseases, mostly dengue, clinically difficult [2]. It is transmitted by the *Aedes* species mosquitoes, but transmission may also occur sexually and transplacentally [3], and has been recently associated with congenital neurologic birth defects in countries of South and Central America [4–7]. Since most of the population of the planet lives in areas infested by *Aedes* mosquitos, including southern Europe, and infection by ZIKV is usually asymptomatic or mildly symptomatic, it is obvious that ZIKV infection poses a public health threat, even for countries far away from South and Central America.

## Case report

A newly married man and woman were examined in November 2016 at the Infectious Diseases Clinic of University hospital of Heraklion in Crete island, Greece, 24 h after returning from their honeymoon in Cuba. The woman reported sudden onset of fever, malaise, headache, myalgias and a skin rash on her torso on the sixth

day of her stay in Cuba, for which she was admitted in a local hospital and was discharged 24 h later in order to return to Greece. The man reported only fever and a mild skin rash, which he omitted to inform the doctors in Cuba. Upon presentation, they were both afebrile. The man had an unremarkable physical examination, while the woman had mild non-tender cervical lymphadenopathy. Due to their recent travel to the Caribbean and their symptoms of fever and rash, serology and reverse transcription PCR (RT-PCR) were ordered for flaviviruses on the 8th day from the symptom onset, during a second visit in our clinic one week later. Zika virus (ZIKV) RNA was detected in woman's first samples of blood and urine; the PCR was still negative in the blood taken one week later (Table 1). ZIKV RNA was also detected in man's urine taken upon first examination, while it was not anymore detectable one week later (16th day from woman's symptoms onset) implying a lower viral load. Additionally, the real time RT-PCR was negative for Dengue virus (DENV) and Chikungunya virus (CHIKV). The serological results were also indicative of an acute ZIKV infection in both patients. Cross-reactivity with DENV was seen, while the detection of DENV IgG antibodies in the woman is additionally explained by cross-reactivity with yellow fever virus for which she was vaccinated in 2010 (Table 1). The Hellenic Center for Disease Control and Prevention was notified, the couple's neighborhood in Greece was disinfected in order to eliminate mosquitoes, and advice was given to the couple for protected sexual contact, as well as avoidance of pregnancy for at least six months

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**Table 1**

Laboratory serological and molecular results from the examination of the blood and urine samples from the newlywed couple upon examination at the Infectious Diseases clinics (1st sample) and one week later (2nd sample).

	Woman 1st sample	Woman 2nd sample	Man 1st sample	Man 2nd sample
ZIKV IgM cut-off: 1.1	4.06	3.06	4.42	2.2
ZIKV IgG cut-off: 1.1	Negative	1.45	Negative	1.98
DENV IgM cut-off: 1	3.87	2.47	2.21	1.20
DENV IgG cut-off: 1	Positive	Positive	1.3	2.35
DENV-NS1 Ag cut-off: 1	Negative	ND	Negative	ND
Real time RT-PCR ZIKV in blood	Positive	Positive	Negative	Negative
Real time RT-PCR ZIKV in urine	Positive	Negative	Positive	Negative
Real time RT-PCR DENV in blood	Negative	ND	Negative	ND
Real time RT-PCR DENV in urine	Negative	ND	Negative	ND
Real time RT-PCR CHIKV in blood	Negative	ND	Negative	ND
Real time RT-PCR CHIKV in urine	Negative	ND	Negative	ND

after their return from Cuba.

## Discussion

ZIKV has recently emerged as an important cause of congenital neurologic birth defects, and, more specifically, microcephaly, after the occurrence of an outbreak in Brazil in 2015, which caused a twenty-fold increase in microcephaly cases at that time [4–7]. Since then, many confirmed ZIKV infections have been imported from Central and South America and the Caribbean [8–10]. Herein, we report the first two cases of ZIKV infection in Greece, the southeastern border of Europe. Greece is a non-endemic country regarding ZIKV. Nevertheless, the region is infested with mosquitoes of the genus *Aedes*, like *Aedes albopictus* [11], which could serve as vectors for ZIKV. This could imply the possibility of establishing a mosquito population capable to cause autochthonous cases.

The two infected patients were newly married and travelled for honeymoon to Cuba where ZIKV is endemic. ZIKV poses a worrisome threat for people of reproducing age, who are the ones that mostly take advantage of the diminished distances current travel modalities offer. Indeed, through 27 March 2017, 2,141 cases of ZIKV infections were documented in the European Union, while 108 of those were in pregnant women [11]. As such, the spread of ZIKV poses an important threat to public health, even for distant European countries. This is not adequately managed by educating potential travelers to areas where ZIKV is endemic to avoid exposure to mosquitoes, or by screening returning travelers for arboviral infections based on the presence of symptoms, since avoidance of this day feeding mosquito is quite difficult and testing all symptomatic returning travelers from endemic areas for ZIKV antibodies and RNA would neither be a viable option from a financial perspective, nor it would not be quite effective either, since ZIKV infection can present with minimal symptoms [12]. Thus, the possibility of infection of a person in reproductive age in Europe leading to transplacental transmission of ZIKV to the fetus in the event of a pregnancy, even months after travel, could not be effectively ruled out, even if the woman is not the returning traveler, due to the long-term persistence of ZIKV in semen [12,13]. This has clear implications for public health, urging the implementation of family planning education as a method of eliminating the possibility of neurological complications at the fetus in the event of a pregnancy.

In conclusion, ZIKV infection poses a threat for public health

worldwide, since travelers to areas where ZIKV infection is endemic could be asymptomatic carriers of the virus, leading to risk of neurologic birth defects for their offspring, as well as increased risk of infestation of the virus to mosquitos of their country, having as a consequence the establishment of nests of ZIKV persists even in countries very far from the ones that the ZIKV epidemic first occurred.

## Consent

Written informed consent was obtained from the patients for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

## Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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