



BRIEF COMMUNICATION

Travelers With Chikungunya Virus Infection Returning to Northwest Italy From the Caribbean and Central America During June–November 2014

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Chikungunya virus (CHIKV) has recently emerged in the Caribbean. In Italy, CHIKV vector is documented in the Po river valley; therefore, a risk for autochthonous outbreaks is present. We report a case series of seven imported CHIKV infections in travelers returning from the Caribbean and Latin America occurring between June and November 2014, in the area of Turin, Northwest Italy, 3 years after the last imported cases were reported. These cases are a reminder of the need to always consider CHIKV infection in travelers from these epidemic areas as well as the importance of a prompt diagnosis.

During the last decade, Chikungunya virus (CHIKV) spread from Kenya to the islands of the Indian ocean and India, and then to the Pacific ocean and French Polynesia.¹ In the year 2013, CHIKV emerged as an important threat in the Caribbean islands, the Dominican Republic, and Haiti; in December 2013, the Pan American Health Organization (PAHO) and the World Health Organization (WHO) confirmed the first cases of autochthonous CHIKV transmission in Saint Martin.^{2,3} During the year 2014, the virus spread to Central and South America, where it caused widespread outbreaks.^{2–4} In European temperate countries, the threat of reintroducing CHIKV and the development of autochthonous outbreaks are high due to the presence of the competent vector, *Aedes albopictus*, as demonstrated by the Italian and French CHIKV outbreaks in the years 2007 and 2010, respectively, and the recently reported cases of CHIKV fever (CHIKF) in South France.^{5–7} In Italy, after the 2007 outbreak, no further autochthonous cases of CHIKF were reported, but in the northern part of the country along the Po

river valley, the presence of the vector poses a serious risk for potential new outbreaks.⁸ Epidemiological surveillance is crucial to identify imported cases and introduce measures to reduce mosquito density. In Italy, since the year 2007, a national surveillance plan for CHIKF has been implemented and recent data from the Italian Ministry of Health showed that in the last few years (2011–2013), CHIKF occurred only as sporadic imported cases.⁹

Herewith, we report a case series of seven travelers with CHIKF returning from the Caribbean and Latin America who were referred to the regional center for infectious diseases, Amedeo di Savoia Hospital, Turin, Northwest Italy (4 million inhabitants), between June and November 2014. These are the first imported cases of CHIKF in Northwest Italy since the year 2011 and are a reminder that CHIKF should be considered in travelers with fever returning from the Caribbean and Central America where the virus has recently become epidemic.¹⁰

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Case Series

A total of 51 serum samples from 44 Italian febrile travelers were studied after hematological, biochemical, microbiological, and virological examinations to rule

Table 1 Characteristics of Chikungunya virus fever in a case series of seven travelers from endemic areas

ID	Country visited	Duration of stay (days)	Sex	Age (years)	IgM (titer)	IgG (titer)	CHIKV RNA	Days from symptoms onset	Clinical symptoms
1	Haiti	30	F	56	+ (1:320)	+ (1:1,000)	–	20	Fever, arthralgia, myalgia, rash, itching
2	Dominican Republic	10	M	46	+ (1:320)	–*	–	7	Fever, arthralgia, myalgia, rash, abdominal pain, diarrhea
3	Dominican Republic†	30	F	56	+ (1:640)	+ (1:3,200)	–	30	Fever, arthralgia, myalgia, headache with retro-orbital pain, abdominal pain, diarrhea, vomiting, itching
4	Martinique	Na	F	53	+ (1:320)	+ (1:100)	–	12	Fever, arthralgia, rash, abdominal pain, diarrhea
5	Dominican Republic	30	F	47	+ (1:320)	+ (1:320)	–	15	Fever, arthralgia, myalgia
6	El Salvador	Na	F	46	+ (1:320)	+ (1:320)	–	10	Fever, arthralgia, rash
7	Dominican Republic	30	M	63	+ (1:320)	+ (1:320)	–	10	Fever, arthralgia, arthritis

Specific CHIKV-reactive results by serological testing were confirmed on further serum samples. Data were retrieved from medical records and the local surveillance system.

F = female; M = male; Na = not available.

*IgG seroconversion from negative to positive (1:640) in a sample collected 2 weeks later.

†Hospitalized.

out tropical diseases due to *Plasmodium* spp., dengue virus, CHIKV, hepatitis A virus, *Salmonella* spp., and other parasitic or non-tropical febrile illness.

Specific IgG and IgM antibodies to CHIKV were detected with a commercial immunofluorescence assay (Euroimmun, G). CHIKV RNA was investigated with the LightCycler® (Roche Diagnostics, Indianapolis, IN, USA) real-time polymerase chain reaction (PCR) with the E1 gene (TIB MOLBIOL GmbH, G), after nucleic acid extraction from 0.5 mL of plasma with the NucliSENS easyMAG (BioMérieux, Marcy l'Etoile, France). PCR sensitivity, according to standard CHIKV preparations from the European Network for Diagnostics of Imported Viral Diseases (www.enivd.de), was 300 copies/mL. Blood samples were processed for serology and molecular tests according to strict safety procedures in the BSL3 Unit of the laboratory of Virology.

CHIKF was identified in 7/44 patients (16%) by specific IgM reactivity (Table 1). Six patients were also IgG positive. Only the patient without specific IgG (Table 1, ID#2) seroconverted to IgG positive in a second serum sample taken 2 weeks later. Viral RNA was negative in all patients.

Travelers returned to Italy from the Dominican Republic ($n=4$), Martinique ($n=1$), Haiti ($n=1$), and El Salvador ($n=1$). Three of them were living in Italy, but born in the Americas (one in El Salvador and two in Santo Domingo, Table 1, ID#3, ID#5, ID#6); four were born and living in Italy. None was a tourist worker. Average duration of the stay in CHIKV-epidemic countries was 26 ± 9 days (range 10–30 days). Major clinical manifestations were fever and severe arthralgia-myalgia-arthritis in all patients, skin rash

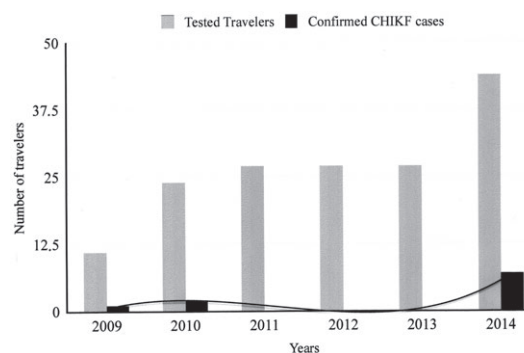


Figure 1 Number of travelers tested and confirmed for Chikungunya virus as reported by the regional reference center for infectious diseases, at the Amedeo di Savoia Hospital, Torino, Italy, from the year 2009 to 2014. CHIKF = Chikungunya virus fever.

(five patients, 71%), abdominal pain and diarrhea (three, 43%), itching (two, 29%), and headache with retro-orbital pain and vomiting (one, 14%). Blood count was normal in all of them. All patients underwent supportive therapy, and only one (ID#3) was hospitalized due to persistent polyarthralgia.

Local laboratory, clinical, and surveillance records from the year 2009 to 2013 were reviewed. Only isolated CHIKF cases were observed in 2009 ($n=1$) and 2010 ($n=2$); no cases were reported from 2011 to 2013 (Figure 1). As can be seen in Figure 2, temporal distribution of the 2014 CHIKF cases coincided with the activity period of *A. albopictus* circulation in Italy from June to November (Figure 2).¹¹

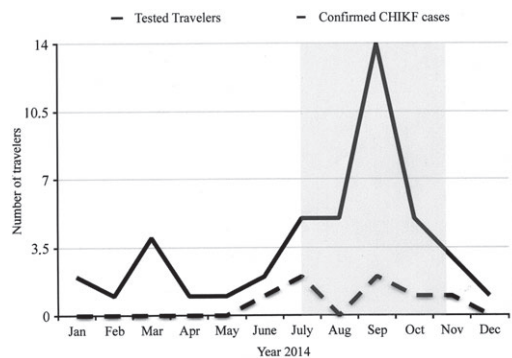


Figure 2 Chikungunya virus fever tested and confirmed cases by month in the year 2014 (the gray area represents the activity period of *Aedes albopictus* circulation and distribution in Italy, from June 14 to November 14).

Travelers without CHIKF ($n=37$) were diagnosed with dengue infection ($n=5$, 14%), malaria ($n=2$, 5.5%), acute hepatitis A ($n=1$, 3%), recently acquired HIV infection ($n=1$, 3%), pneumococcal pneumonia ($n=1$, 3%), leptospirosis ($n=1$, 3%), Epstein–Barr virus ($n=1$, 3%), and cytomegalovirus infection ($n=2$, 5.5%); in 23 cases, no diagnosis was made.

Discussion

The rapid spread of CHIKF in the Caribbean and Central America is an increasing worldwide concern.^{1,12} In Europe, where the competent vector is present, recent data underline the high prevalence of CHIKF in travelers returning from epidemic countries and the need for prompt diagnosis and response as viremic patients could be a potential source of autochthonous outbreaks.^{7,10} In Italy, *A. albopictus* was first introduced during the 1990s, then spread across the country and is currently commonly found in North Italy below 600 m of altitude.⁵ After the autochthonous outbreaks in 2007, an integrated national health surveillance system for CHIKF with the entomological control of the vector over the country is active.

Italian National reports show that during the years 2011–2013, the majority of Italian regions reported CHIKF only as sporadic imported cases. We report a case series of CHIKF in travelers returning from the Caribbean and Central America to Northwest Italy during June to November 2014, after 3 years without imported cases of CHIKF in this region. A failure of the local surveillance system during these years is rather unlikely, even if underestimation of a very rare disease, such as CHIKF, so far in our country, cannot be totally excluded.^{9,12}

CHIKF was diagnosed a mean of 17.7 days after fever onset (range 7–30 days) with serological tests that show reactivity for specific IgM in all patients, while no patient was viremic, probably due to the time elapsed between symptom onset and blood collection, as also confirmed by the presence of IgG antibody in the

majority of patients. Molecular tests for the detection of viral RNA are most useful for the early presentation of the disease (within the first 7 days after symptom onset). For late presentations, IgM testing is mandatory. Recent studies on CHIKV protein characterization showed that it is possible to design more sensitive serological assays using specific early phase E2 glycoprotein as antigens.¹³

In conclusion, our findings are in line with the Italian National CHIKV surveillance system preliminary report for the year 2014 and European data,^{4,10,12,14,15} outlining the recent increasing frequency of imported CHIKF due to the Caribbean and Central America spread of the virus and how important are regional, national, and European surveillance reporting systems.^{4,10,12,14,15} Returning travelers are sentinels of a rapidly changing epidemiology and require a prompt diagnosis and a careful surveillance for their implication in subsequent autochthonous transmission of the disease.¹² Therefore, in non-endemic countries, health care providers should improve the understanding of CHIKF clinical spectrum when managing returning travelers.

Acknowledgments

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Declaration of Interests

The authors state that they have no conflicts of interest.

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This village is characteristic of those standing along the northwestern coast of Italy, the area where the study by Burdino et al. was performed. More particularly, this village is one of the most beautiful amongst the five of the “Cinque Terre”, Liguria. Setting: Manarola, Italy. *Photo Credit: Eric Caumes.*