

# Four-year surveillance of imported Dengue virus infection in Italy North-West



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## Background:

Today, Dengue is regarded as the fastest-growing vector borne disease worldwide. We evaluated the epidemiology of imported Dengue in Piemonte, North-West Italy (4,2 million inhabitants), in travelers returning from endemic areas, between January 2012 and November 2015. The geographic area is characterized by the presence of Dengue vector *Aedes albopictus* with a high risk of autochthonous cases.

## Materials/methods:

Blood samples (n=319) from 100 Italian febrile travelers from Dengue endemic areas referring to the regional Centre for Infectious Diseases, Amedeo di Savoia Hospital, Turin, North-West Italy were studied. Patients underwent hematological, biochemical, microbiologic and virological examinations to rule out a tropical fever. Investigation of Dengue virus specific IgG and IgM antibodies was made by ELISA (NovaLisa Dengue IgG/IgM ELISA, D). DENV RNA was investigated with the Fast-track diagnostics Dengue/Chik PCR-based assay; on RNA-positive samples Dengue serotype was identified with a Dengue differentiation molecular test (Fast-track diagnostics Ltd., Luxembourg). From January 2015, rapid test to NS1 antigen was introduced (Panbio ALERE, I).

## Results:

Acute/recent DENV infection was identified in 53 out of 319 (16.6%) travelers from endemic areas including 43 primary and 10 secondary infections; 18 out of 53 (34%) positive travelers were viraemic and Dengue typing was performed in 16 of them with type 1 being the most prevalent one (DENV-1, n=7, 38.9%; DENV-2, n=2, 11%; DENV-3, n=4, 22%; DENV-4, n=3, 16.7%). In 35 patients the diagnosis of DENV infection was accomplished by the combination of specific IgM reactivity, high IgG titers, IgG seroconversion from negative to positive and increasing (four-fold) IgG titers in paired serum samples. In the year 2015, with the introduction of NS1 rapid test, Dengue antigen was detected in 9 out of 16 patients (56%), the majority of them (n=8) with positive RNA by PCR. Patients were returning to Italy from the Caribbean area (n=28) or South East Asia (n=24) and 1 from Congo.

Main clinical manifestations were fever (all patients), followed by joint and muscle pain (51% of patients), headache (34%), skin rash (30%) and diarrhea (13.2%); leukopenia was present in 41.5% and thrombocytopenia in 20.8% of travelers. All patients underwent supportive therapy and recovered within few weeks from the diagnosis. Hospitalization occurred in 14/53 patients (26.4%).

**Table 1.** Acute/recent DENV infection: virologic and serologic status of the 53 travelers.

Travelers (n.)	Acute/recent DENV infection			
	DENV-RNA	IgM	IgG	NS1 Ag
24	-	+	+ <sup>a</sup>	
3	-	+ <sup>b</sup>	-	
3	+	-	-	
4	+	+	-	
3	+	+ <sup>c</sup>	+ <sup>c</sup>	
<b>Rapid test from 2015</b>				
1	-	+	-	+
4	-	+ <sup>d</sup>	-	-
3	-	+	+	-
6	+	+ <sup>e</sup>	+ <sup>f</sup>	+
2	+	+	-	+
<b>Tot. 53</b>				

<sup>a</sup> IgG seroconversion from negative to positive in 4/24 travelers. In 10 patients high IgG titer (1:1000 with IIF assay) and IgM reactivity or high IgM titer (>200) and IgG reactivity were suggestive of DENV infection.

<sup>b</sup> High IgM titer (>200) and IgM seroconversion from negative to positive in 2/3 pts.

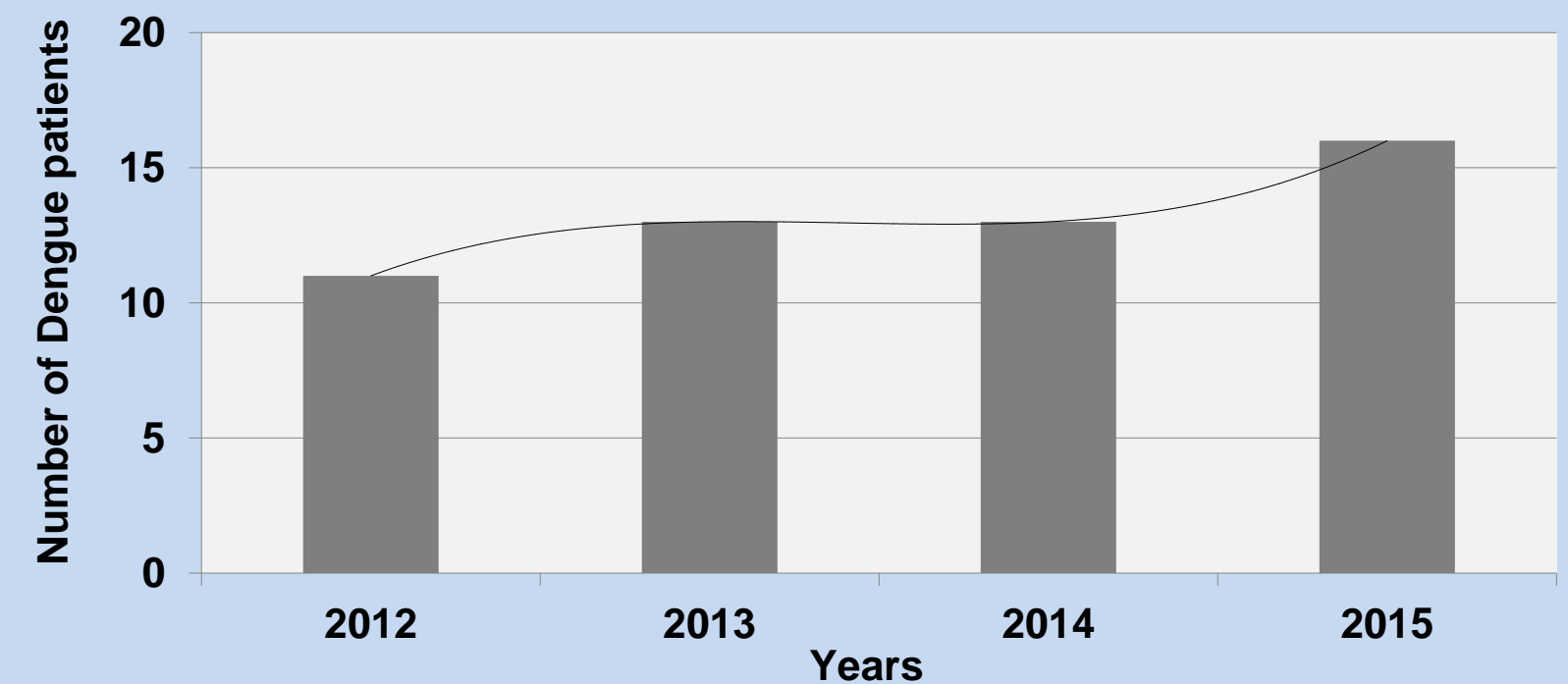
<sup>c</sup> IgM and IgG seroconversion from negative to positive in 3/3 pts.

<sup>d</sup> Confirmed by high IgM titer (>200) and IgM seroconversion from negative to positive in 2/4 pts.

<sup>e</sup> IgM seroconversion from negative to positive in 4/6 pts.

<sup>f</sup> IgG seroconversion from negative to positive in 2/6 pts.

**Figure 1.** Number of imported Dengue fever in the period of time 2012-2015.



**Table 2.** Dengue virus typing.

Travelers (n.)	DENV- 1	DENV- 2	DENV- 3	DENV- 4	Untyped
18	7	2	4	3	2

## Conclusions:

Returning travelers are sentinels of a rapidly changing epidemiology and require a prompt diagnosis and a careful surveillance for their implications in subsequent autochthonous transmission of the disease. Our findings outline the high rate of imported Dengue infection in North West Italy and emphasize the need of a continued Dengue surveillance in non-endemic countries as well as a careful evaluation and follow-up of febrile patients returning from Dengue endemic areas.