Prevalence of Toscana virus antibodies in residents of Croatia

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Abstract

To assess the prevalence of Toscana virus (TOSV) infection among healthy residents of Croatia we tested sera from 2016 persons, for IgG antibodies to TOSV, by an enzyme immunoassay. A total of 755 (37.5%) persons had IgG antibodies to TOSV: 53.9%, 33.6% and 6.1% among residents of the islands, coastal area and mainland of Croatia, respectively. Risk factors significantly associated with seropositivity to TOSV were: living on islands (OR, 11.10; 95% CI, 6.02–20.50; p <0.001) or in coastal areas (OR, 6.96; 95% CI, 3.81–12.71; p <0.001) and increase of age (OR, 1.03; 95% CI, 1.02–1.03; p <0.001).

Keywords: Croatia, Phlebovirus, seroprevalence, Toscana virus

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Toscana virus (TOSV) (family Bunyaviridae, genus Phlebovirus) is an arbovirus transmitted by sandflies (Phlebotomus spp). TOSV is neurovirulent and causes aseptic meningitis during the summer time in both residents of and travellers to Mediterranean countries [1–4].

No information on TOSV circulation in Croatia is available. The aim of this study was to determine the prevalence of TOSV antibodies among the healthy population of different regions in Croatia.

Croatia is situated between central and south-eastern Europe, lying along the east coast of the Adriatic Sea (Fig. 1). The Croatian littoral is composed of the northern (Istria and Primorje) and southern part (Dalmatia), which is subdivided into northern, central and southern Dalmatia. The Adriatic coast and islands are characterized by the Mediterranean climate, which is favourable for maintaining sandfly vectors of TOSV [5]. The mainland parts of Croatia, which have the continental climate, are considered sandfly-free areas.

From 2007 to 2009 we collected blood specimens from 2016 healthy inhabitants of island, coastal or continental parts of Croatia, aged 8 months to 88 years, who came to hospital for laboratory check-ups or blood donation. Information regarding age, gender and site of residence was collected. The ethical committee of Split University Hospital approved the study.

Presence of anti-TOSV IgG was investigated using a commercial enzyme immunoassay (rEIA, Enzywell Toscana Virus IgG/IgM, DIESSE, Siena, Italy). Previous studies of rEIA had revealed its sensitivity and specificity for IgM to be 100%, and for IgG to be 100 and 96.6%, respectively [6].

The data were analyzed using SPSS version 19.0. Chi-square tests, odds ratios (OR) and multiple logistic regression were used to estimate associations with seropositivity and to evaluate potential risk factors for TOSV infection.

Of the total of 2016 sera, anti-TOSV IgG were found in 755 (37.5%). Seroprevalence differed significantly among sites, ranging from 4.7% in Brod-Posavina County to 67.7% on the island of Lastovo (Fig. 1, Table 1). Islanders were more seropositive than inhabitants of coastal (v2 = 69.82, p <0.001) or mainland areas (v2 = 139.33, p <0.001). Inhabitants of coastal areas were more seropositive than those from mainland regions (v2 = 61.46, p <0.001).

Prevalences among the coastal and continental counties, as well as between the islands, were compared (Table 1). With regard to islands data, a decrease in risk of TOSV infection was determined for the northern-most islands of Istria and Primorje (Fig. 1) relative to islands of central (OR = 0.52; 95% CI, 0.33–0.84; p 0.007) or southern Dalmatia (OR = 0.61; 95% CI, 0.35–1.04; p 0.070 borderline significance).

All endemic sites (coastal or island) had significantly higher risk of TOSV infection, compared with the continental counties (OR from 6.46 to 21.39; p <0.001).

An increased probability of acquiring the infection with age was observed. Seroprevalence rate increased from 10.2% in
children 0–9 years old to 70.7% in people over the age of 70, thereby increasing the risk of infection up to OR of 16.42.

Multivariate logistic regression found that older age and living on the coast or an island to be significantly associated with seropositivity to TOSV (Table 1).

To the best of our knowledge, this is the first study of prevalence of TOSV antibodies in Croatia. In order to determine the TOSV infection distribution, residents of various geographical areas were included in the study. Two counties in continental Croatia, which are not considered endemic for sandflies, were studied for comparison. The commercial rEIA test was used because many TOSV seroprevalence studies were based on this test [3,7–13].

As we presumed, the seroprevalence was significantly lower in residents of continental areas of Croatia. As people from the mainland often travel to the Croatian littoral for summer vacations, we cannot exclude the possibility of them being infected there. It is known that in people visiting endemic areas TOSV infections may occur without any signs of illness [3,4,13,14]. One could also speculate that autochthonous TOSV infection may occur due to the observed spread of sandflies to the central European region [1,14,15].

TOSV infection is found throughout the Croatian littoral stretching from Istria to the Montenegro border. Observed seroprevalence appears to be variable according to the geographical site of study. Similar dispersal patterns, which

**FIG. 1** Map of Croatia showing the geographical distribution of Toscana virus seroprevalence.
correlate with favourable habitat for sandflies, have been observed in other Mediterranean countries [8,11,16]. The mean prevalence in the coastal zones was 33.6%, with the highest prevalence of 39.9% in southern Dalmatia. Between different islands the mean seroprevalence rate was 53.9%, with the lowest prevalence being 19.2% on the island of Cres. Residents of central and southern Dalmatia islands were significantly more likely to be TOSV seropositive than residents of the northern islands. The prevalence of antibody to TOSV on the island of Lastovo, the most outlying island of Croatia (67.7%), is among the highest in Mediterranean countries. A similar prevalence of 61.0% was found on the Spanish island of Mallorca [16] and lower prevalence from 39% to 51.7% was found among inhabitants of two Greek islands [11].

Data from seroepidemiological studies conducted in other Mediterranean countries have also shown a variable prevalence of TOSV infections depending on the geographical regions and other risk factors [1–4,7–13,16–18]. The highest seroprevalence (77.2%) reported to date was observed among forestry workers in the endemic zone of Tuscany, Italy [4,8].

In our study the frequency of antibodies increased with age, suggesting regular exposure to TOSV through time. The recent circulation of TOSV in the region is evident from the presence of antibodies in the serum of a 1-year-old girl from southern Dalmatia and in 10.2% of sera of children under the age of 9. The age-dependent increase was also observed in other studies [4,7–11].

In conclusion, our results have shown that the Croatian littoral areas are endemic for TOSV. Physicians should be aware of the circulation of TOSV, which must be considered as an aetiological agent in cases of summer aseptic meningitis in local residents as well as in travellers to the region. Further studies including clinical, virological and entomological investigation are needed for elucidating the role of TOSV in public health in Croatia.

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Transparency Declaration

The authors report no conflicts of interest.

References


