International Journal of Infectious Diseases 64 (2017) 20–26

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Spatial distribution of West Nile virus in humans and mosquitoes in Israel, 2000–2014

Yaniv Lustig[a,1,*], Zalman Kaufman[b,1], Ella Mendelson[a,c], Laor Orshan[d], Emilia Anis[e,f], Yael Glazer[e,g], Daniel Cohen[c], Tamy Shohat[a,c], Ravit Bassal[b]

[a] Central Virology Laboratory, Ministry of Health, Chaim Sheba Medical Center, Tel-Hashomer, Israel
[b] Israel Center for Disease Control, Ministry of Health, Chaim Sheba Medical Center, Tel-Hashomer, Israel
[c] Department of Epidemiology and Preventive Medicine, School of Public Health, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel
[d] Laboratory of Entomology, Ministry of Health, Jerusalem, Israel
[e] Division of Epidemiology, Ministry of Health, Jerusalem, Israel
[f] Braun School of Public Health, Hebrew University and Hadassah, Jerusalem, Israel
[g] Department of Public Health, Ben-Gurion University of the Negev, Beer-Sheva, Israel

ARTICLE INFO

Article history:
Received 6 July 2017
Received in revised form 9 August 2017
Accepted 26 August 2017
Corresponding Editor: Eskild Petersen, ?Aarhus, Denmark

Keywords:
West Nile virus
Prevalence
Mosquitoes
WNV infection
Spatial distribution
Israel

ABSTRACT

Objectives: Israel has a long history of West Nile virus (WNV) morbidity, and the rate of detection of WNV in mosquitoes has been high since 2000. The aim of this study was to integrate several WNV datasets in order to gain an insight into the geographical distribution of WNV in Israel.
Methods: Three choropleth maps were generated showing WNV human morbidity, WNV prevalence in mosquitoes, and the results of a nationwide serological survey, based on the division of Israel into 15 sub-districts.
Results: The maps show a high endemicity of WNV in Israel. In respect to the morbidity map, the population residing in the central part of the country and in Arava Region is at higher risk of developing the disease than the population of the rest of Israel. Interestingly, high prevalence rates of both WNV serology and WNV-infected mosquitoes were detected in Arava Region, but lower prevalence rates were detected in most areas of the coastal region, suggesting that other factors might also be important in the development of symptomatic WNV infections.
Conclusions: These results underline the high prevalence of WNV in Israel and point to specific risk areas for WNV infections across the country.

Introduction

West Nile virus (WNV) is a vector-borne flavivirus whose reservoir includes many species of birds, and the virus is primarily transmitted by Culex mosquitoes (Go et al., 2014). Approximately 80% of WNV infections in humans have no symptoms and 20% cause a mild febrile illness termed West Nile fever (WNF). However, approximately 1% of cases are much more severe, leading to West Nile neuroinvasive disease (WNND) (Kramer et al., 2008). Several WNV outbreaks with high numbers of WNND cases have occurred in animals and humans in Europe, the Middle East, and North America since the 1990s (Anis et al., 2014; Bin et al., 2001; Calistri et al., 2010; Hernandez-Triana et al., 2014; Murray et al., 2010).

WNF has been known in Israel since the early 1950s. The virus was responsible for several outbreaks occurring in that decade and an additional outbreak in 1980 (Anis et al., 2014). Following a massive outbreak in geese in 1998–1999, a large-scale human outbreak occurred in 2000, with more than 400 confirmed cases and nearly 40 fatalities (Anis et al., 2014; Bin et al., 2001; Weinberger et al., 2001). Since then, outbreaks of varying magnitude have frequently been recorded, with nearly 1400 cases of WNF and WNND reported in Israel between 2000 and 2012 (Anis et al., 2014). Furthermore, several studies conducted on specific study populations have demonstrated high WNV IgG seroprevalence in Israel (Bin et al., 2001; Chowers et al., 2005; Cohen et al., 1999). A nationwide cross-sectional serological survey recently

* Corresponding author at: National Center for Zoonotic Viruses, Central Virology Laboratory, Ministry of Health, Sheba Medical Center, Ramat-Gan, Israel. Fax: +972 3 5302457.
E-mail address: Yaniv.lustig@sheba.health.gov.il (Y. Lustig).
[1] Yaniv Lustig and Zalman Kaufman contributed equally.

https://doi.org/10.1016/j.ijid.2017.08.011

conducted by the Central Virology Laboratory (CVL) and the Israel Center for Disease Control, found an overall WNV seroprevalence of 11.1% in Israel (Bassal et al., 2017). Importantly, despite the geographic diversity of the country, this previous study divided Israel into only seven regions, thus the differential WNV seroprevalence across Israel was only broadly characterized.

Following the 2000 outbreak, a national mosquito surveillance system was established in Israel (Orshan et al., 2008). This system detects WNV-positive mosquitoes and characterizes their WNV genotypes. Overall, 336 mosquito pools were positive for WNV infection from 2000 to 2014, demonstrating the high circulation of WNV in Israel (Lustig et al., 2015); however the geographic distribution of WNV-infected mosquitoes was not assessed.

The geographic position of Israel between three continents makes it an important transit zone for migratory birds. Therefore the analysis of WNV in mosquitoes and geographic information regarding acute WNV infection in Israel, as well as exposure of the general population, could provide valuable information on WNV circulation not only in Israel but also in the entire Mediterranean basin. This study was performed to characterize WNV morbidity, WNV seroprevalence, and WNV-infected mosquitoes in Israel geographically.

Materials and methods

Laboratory investigation and definition of West Nile disease (WND)

The CVL performs diagnostics and also receives information for all WNV-infected patients diagnosed in the CVL and in other hospitals in Israel. This information is transferred to the relevant regional health districts, which then complete an epidemiological investigation of the patients and report the results through a nationwide surveillance system to the Division of Epidemiology of the Ministry of Health. Data collected in this manner are restricted to new cases of WNF with a severe illness that requires hospitalization.

In this study, the place of infection was considered the patient's residence, due to difficulty obtaining sufficient information on the suspected place of exposure for each patient from the case investigations. The detection of IgM and IgG antibodies against WNV in serum and cerebrospinal fluid (CSF) samples was performed by enzyme-linked immunosorbent assay (ELISA). Samples obtained during the years 2001–2007 were investigated using an assay developed in the CVL. Samples obtained during the years 2008–2013 were investigated using commercial IgM and IgG kits (West Nile Detect ELISA; InBios International, Inc., Seattle, WA, USA). Finally, samples obtained in 2014 were assessed by WNV IgM capture (DxSelect ELISA and IgG DxSelect ELISA kits; Focus Diagnostics Inc., Cypress, CA, USA).

Mosquito surveillance

Mosquito trapping and collections were carried out by the Pest Control Unit of the Ministry of Environmental Protection. Trapping sites varied according to the location of mosquito breeding sites and their relevance to control activities, as well as information on WNF cases, and was contingent on the personnel employed. It was not always possible to collect mosquitoes repeatedly from the same localities. Mosquito processing and WNV identification was performed exactly as described previously (Lustig et al., 2015). During the period 2000 to 2014, 7135 pools containing a total of 277 186 mosquitoes arrived at CVL for the detection of WNV RNA. Using TaqMan RT-PCR for the envelope protein, WNV RNA was detected in 336 (4.71%) of the total pools analyzed.

Choropleth maps

ArcGIS 10.4.1 (ESRI, Redlands, CA, USA) was used to create choropleth maps to present WNV morbidity, seropositivity, and mosquitoes positive for WNV at the sub-district level in Israel. Officially, Israel is divided into 15 sub-districts. For the purposes of this study, the respective polygon of Be'er Sheva sub-district (the most southern sub-district of Israel) was split into two regions based on its sub-divisions (seven natural areas): (1) Arava Region, comprising the south-eastern part of Be'er-Sheva sub-district, and (2) the other six natural areas. This was done in order to represent the studied attributes of this specific region more accurately. The following aspects were considered when taking this action: (1) Arava Region lies along the Rift Valley (one of the main routes for bird migration during the spring and autumn seasons) and is known to be highly endemic for WNF, (2) Be'er-Sheva sub-district as a whole is sparsely populated (the population of Arava Region constitutes about 9% of the overall population of this sub-district), and (3) computing rates based on the overall population of Be'er-Sheva sub-district would dilute the effects characteristic of Arava Region.

Results

WNF has been a notifiable disease in Israel since 2001. During the years 2001–2014, 1233 patients were diagnosed with an acute WNV infection in Israel, with an overall annual infection rate of 1.29 per 100 000 across Israel. In order to determine whether certain areas of Israel are more prone to acute WNV infection, the geographical distribution of WNV morbidity in Israel was studied at the sub-district level in this study (see Materials and methods) in terms of annual average rates over this period, using the population data for the year 2006 as the denominator (Figure 1). High morbidity rates were found in Arava Region (5.4 cases per 100 000 per year), as well as in the central part of the country (from Rehovot sub-district to Haifa sub-district (range 1.27–2.43 cases per 100 000 per year)).

Since WNV seroprevalence data reflect exposure of the general population to WNV, these have added value for assessing the spatial distribution of WNV in Israel. In order for the data to reflect long-term exposure and be less influenced by annual fluctuations in WNV infection dynamics, only seroprevalence data retrieved from adult persons should be included. Therefore, the results of the WNV seroprevalence survey (Bassal et al., 2017) were reanalyzed and presented as the percentages of seropositivity in persons aged 30 years and above at the sub-district level (Figure 2). Out of 1318 samples tested, 241 (18.3%) were IgG seropositive for WNV. Relatively high prevalence rates were identified in Arava Region in the south (25.3%) and in the sub-districts of Tel Aviv (25.3%), Petah Tiqwa (31.6%), Hadera (25%), Akko (23.2%), and Ashkelon (22.9%).

As mosquitoes serve as the vector of the disease, Figure 3 presents the sub-district geographical distribution of mosquitoes carrying the virus as a percentage of the number of times the mosquito pools were found to be positive for WNV out of the total pools collected during the years 2000 to 2014. The results showed a high level of mosquito infestation with WNV in Arava Region (21.9%).

Discussion

There are on average 70 ± 40 cases of symptomatic WNV infection in Israel per year (Anis et al., 2014), and a high prevalence of Culex mosquitoes (the primary vectors of WNV) has been observed in the country (Orshan et al., 2008). Despite a substantial amount of data on WNV circulation in mosquitoes having been accumulated over the last 16 years (Lustig et al., 2015), studies have