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ScienceDirect
Acta Tropica 103 (2007) 1–13
ACTA TROPICA
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Space–time analysis of the dengue spreading dynamics in the 2004 Tartagal outbreak, Northern Argentina

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Received 25 October 2006; received in revised form 3 April 2007; accepted 7 May 2007
Available online 17 May 2007

Abstract

The spreading dynamic of the 2004 dengue fever outbreak that occurred in Tartagal, Northwestern Argentina, was investigated. A total of 487 suspected dengue cases were recorded and geo-referenced. Maps of daily cases were generated for the 109 days of the outbreak. The epidemic affected the majority of the city within 11 days. The age-distribution of the cases was different from the population age-distribution. The spatio–temporal clustering of the cases was analyzed using Knox test concept. Results of the space and time geo-referencing of the cases showed outbreak spotlights and spreading patterns that could be related to entomologic and epidemiologic factors. An environmental risk prediction model was developed based on a synthetic multi-band image created from LandSat 5 TM satellite image. The potential and limitations of remote sensing data and spatial statistics as landscape epidemiology tools for a dengue surveillance strategy and prevention are discussed.
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Keywords: Epidemic description; Remote sensing; Modeling; Dengue; Argentina

1. Introduction

Dengue is an arboviral disease including four serotypes of *Flavivirus*, Dengue-1, Dengue-2, Dengue-3, and Dengue-4 (DEN-1, DEN-2, DEN-3, and DEN-4) transmitted by mosquitoes, mainly *Aedes aegypti* (Diptera: Culicidae) (Gubler and Kuno, 1997). Dengue Fever (DF) is endemic in most of the Central and South American countries (PanAmerican Health Organization, 2004). In Argentina, the first dengue-like epidemic was recorded between February and March 1916 with 15000 cases (Avilés et al., 1999). Dengue-like epidemics were then reported regularly until the epidemic reported in 1926, affecting the Mesopotamia region and followed by more then 70 years without report of dengue cases (Seijo et al., 2000). In 1955, the *Ae. aegypti* eradication campaign started with a successful eradication reported in 1963 (Avilés et al., 1999). However, as in the other South American countries, the *Ae. aegypti* re-infestation was reported in the northern part of the country in 1986 (Avilés et al., 2003). In April 1997, DEN-2 cases were detected at Orán, Salvador Mazza, Guemes and Tartagal cities in the Salta province. In 1998, the first modern epidemic took place in Salta province, with 359

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doi:10.1016/j.actatropica.2007.05.003

DEN-2 confirmed cases. In 2000, a DEN-1 epidemic was reported in Misiones and Formosa provinces. Both epidemics were most probably originated from imported cases from neighbouring countries. In 2002, 214 DEN-1 cases were detected in Salta, and DEN-3 appeared in Misiones and in 2003, 98 confirmed DF cases were reported in Argentina. The simultaneous circulation of three dengue virus serotypes (DEN-1, 2 and 3) in Northern Argentina and neighbouring countries demonstrates that dengue viruses are becoming endemic in Argentina and increases the risk of dengue hemorrhagic fever (DHF) cases.

Considering that no vaccine is available, the actual prevention program against dengue is based on vector population control. The *Ae. aegypti* breeding sources are removed regularly to eliminate vector larval stages. In Argentina, after the report of a suspected DF case, indoor and/or spatial spraying of ultra low volume (ULV) of a pyrethroid insecticide is sprayed in approximately 400 meters around the case location block. However, new tools and approaches are needed to improve the spatial DF surveillance and control strategies. The use of satellite images in epidemiology analysis allows the identification of key environmental factors such as, temperature, rainfall, and humidity that influence the dynamic of the vectors and the zoonotic hosts of human diseases, as well as their interactions. Since the beginning of remote sensing (RS) technology, studies on vector-borne diseases have focused on identifying and mapping vector habitats (Barnes and Cibula, 1979; Hayes et al., 1985) assessing environmental factors related to vector biology (Rogers and Randolph, 1991, 1993; Kitron, 1998) and studying diseases epidemiology (Linthicum et al., 1999; Murray, 2003) Recent studies investigated the application of RS and spatial analysis techniques to identify and map landscape elements that collectively define vector and human population dynamics related to disease transmission risk (Wood et al., 1992; Glass et al., 1992). Landscape pattern analysis, combined with spatial statistical analysis, will allow the definition of landscape scale predictors of disease risk that could be applied in larger regions where field data are unavailable (Dister et al., 1997; Beck et al., 2000; Tran et al., 2004). This makes RS/geographic information system (GIS) a powerful tool for disease surveillance and intervention programs (Morrison et al., 1998).

In this context, the National Vector Control Coordination from the Argentinean National Health Minister is developing a research program in collaboration with the Argentinean space agency (CONAE) to incorporate RS and GIS as vector and dengue surveillance complementary tools. An international cooperation framework (MATE) was established with the French consortium S2E (spatial surveillance of epidemics). The main objective of this work was to study, throughout an interdisciplinary and inter-institutional initiative, the 2004 dengue outbreak that occurred in Tartagal, Northwestern Argentina, by using RS and GIS elements for a better understanding of the dengue outbreak dynamics, including the effect of the Dengue National Prevention Program.

2. Materials and methods

2.1. Site of the study

The city of Tartagal is located at the base of the Argentinean sub-Andean hills (22°32′S, 63°49′W, 450 m above sea level) at 450 m above sea level, in the Salta province (Fig. 1). The city is distant of 365 km from the city of Salta, capital of the province, and of 55 km from the Bolivian border. Tartagal's urban area covers approximately 15 km^2, with 60585 inhabitants, including several ethnic groups such as native Amerindians (*Instituto Nacional de Estadística y Censos*, 2001). The city is surrounded by subtropical native forests and crops such as, beans, cotton, soybean, maize, grapefruit and tomato. The climate is subtropical, with annual rainfalls of about 1000 mm, means temperatures of about 23° C in spring, 38° C in summer, 14° C in autumn and 9° C in winter, with more than 350 days free of frost annually.

2.2. Dengue cases

After the first DF cases were confirmed, all persons that had visited the Tartagal hospital with the following symptoms: temperature $\geq$ 38 °C, arthralgia, headache, and myalgia, were considered as suspected DF cases and were notified by the "*Sistema Nacional de Vigilancia Epidemiologica*" (SiNaVE) to the National Vector Control Coodination. To estimate the probable and confirmed DF cases, blood samples were taken for approximately half of the suspected cases. The patients visited the hospital spontaneously or were sent by private health centers. The terminology of suspected, probable, and confirmed DF cases was used according to the definitions adopted by *Ministerio de Salud de la Nación Argentina* (*Ministerio de Salud de la Nación*, 1999), and the Center for Disease Control and Prevention (CDC), Atlanta, Georgia (CDC, 1990, 2001). A suspected DF case was defined as an acute febrile illness no longer than seven days, characterized by frontal headache, and showing at

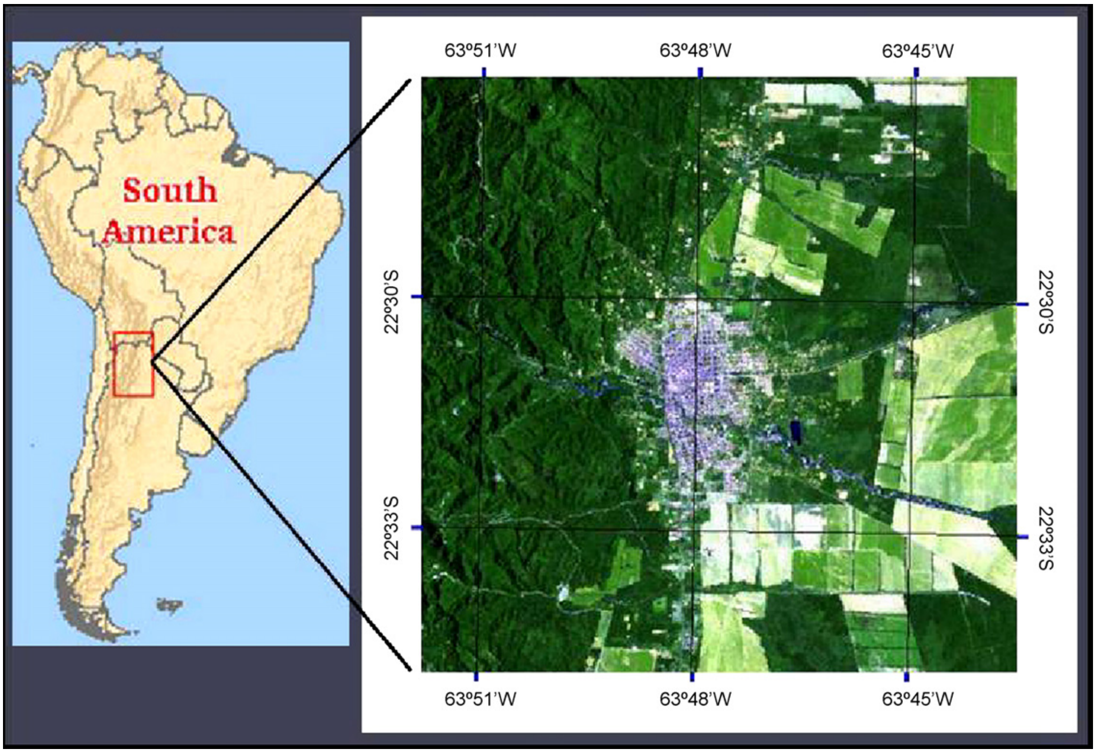

Fig. 1. Geographical location and satellite image from LandSat 5 TM (25th January 2004) of the city of Tartagal.

least two of the following symptoms: retro-ocular pain, muscle and joint pain, rash and minor bleeding phenomena and residence or movement into an area with confirmed DF transmission. A probable DF case was a clinically compatible case with supportive serologic findings such as a single acute or convalescent-phase serum positive for Immunoglobulin (Ig) M antibody or a dengue virus IgG antibody titer ≥ 1280. A confirmed case was a clinically compatible case that was laboratory confirmed either by virus isolation, molecular biology test (PCR), IgM seroconversion or a fourfold increase in IgG titers for paired serum. According to the origin of the DF cases, autochthonous cases were originated from the Tartagal region when transmission was occurring, and imported cases were DF cases originated from different region or country.

In a DF outbreak situation, after virus circulation was confirmed we consider that the predictive positive value for a probable dengue case to be a confirmed case was very high, and all the suspected cases were included in the spatio–temporal analysis. The Ministry of Health of Argentina approved this research program and informed consent was obtained from all adults and parents of children reported as dengue cases, to use their personal data.

2.3. Laboratory investigations on patients' sera

The epidemiological data of the 2004 DF outbreak in Tartagal were obtained from the Ministry of Health of Argentina. The laboratory tests on the serum of the suspected DF cases included: (1) isolation of dengue virus from serum and/or autopsy tissue samples; (2) detection of dengue virus genomic sequences in autopsy tissue, serum samples or cephalo-rachidial liquid using monoclonal antibodies and polymerase chain reaction (PCR) techniques; (3) detection of dengue virus antigen in autopsy tissue by immunohistochemistry or by viral nucleic acid detection; (4) demonstration of a fourfold or greater rise or fall in reciprocal immunoglobulin G (IgG) or immunoglobulin M (IgM) antibody titers to one or more dengue virus antigens in paired serum samples (*Ministerio de Salud de la Nación*, 1999). Acute-phase serum samples (<5 days after onset of symptoms) were sent directly to INEVH (National Institute of Human Virus Diseases) and tested for viral isolation in C6/36 cells or PCR. Late-acute serum samples taken from patients with suspected DF infection (>5 days after onset of symptoms) were tested at provincial laboratories by IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA) (Bundo and Igarashi, 1985) with a commercial kit (ultramicro enzyme-linked immunosorbent assay capture immunoglobulin [Ig] M dengue test, Instituto Pedro Kouri, Havana, Cuba). All positive samples and at least 10% of negative samples were sent to INEVH for quality control and confirmation. At INEVH, samples were tested by MAC-ELISA for IgM antibodies, plaque reduction neutralization test (PRNT), hemagglutination inhibition (HI) test adapted from Clarke and Casals (1958) and immunofluorescence detection (using monoclonal antibodies obtained from PAHO). During the convalescent-phase period, a second sample was obtained from patients with positive results for DF and tested by MAC-ELISA.

2.4. Dengue cases geo-referencing and space–time analysis of the epidemic

The Ministry of Health of Argentina provided a Tartagal cadastral map with the identification numbers used to reference each block in their control activities, and a list of the DF suspected cases' home location at block level, including the dates of the symptoms onset, age and sex. Because of ethico-legal issues, case location was limited to block level. A vector layer containing the center of each block was built and the cases were geo-referenced, associating a DF case to one block. This layer allowed us to calculate case-to-case distances. The government's Tartagal 1:5000 scale cadastral map was scanned and a digital geo-referenced Tartagal map was obtained by the registration of the scanned map using ENVI 4.1 software (ENVI, 2004, http://www.ittvis.com/envi/FeatureTour.asp) and ground control points obtained from a geo-referenced LandSat 5TM satellite image (earth science data interface, at the global land cover facility). We used this base-map to spatially report daily, weekly, monthly and total DF cases and to generate incidence maps.

Based on the Knox test concept (Knox, 1964; Kulldorff and Hjalmars, 1999) the accumulative pairs of points found at a given space–distance (in meters) and time–distance (in days) are counted and compared to the number of random expected cases at these distances within the same intervals. To evaluate the presence of periodicity in the outbreak a Fourier harmonic analysis was generated on a time and space distances histogram (Crist and Kauth, 1986; Mehta et al., 2002).

2.5. Predictive map modeling

The spatial pattern of the dengue outbreak is a cooperative result of multiple factors that can be grouped into environmental, demographic, entomologic and epidemiologic factors among others. These factors may be classified into micro-scale factors (such as mosquito breeding sites), medium-scale factors (such as houses) and macro-scale factors (such as blocks of houses or roads). We intended to explore what percentage of the dengue outbreak spatial pattern was possibly described by macro-scales factors identified through remote sensing techniques. The macro-scale factors included some environmental factors, such as rivers, vegetation, wetness, temperature and some demographic factors such as edifications and roads. Then, this large-scale factors will be called in the text as "macro-habitat factors". The objective of this section was to estimate the effects of macro-habitat conditions (when we say "macro-habitat conditions", we refer to, for example, river nearness, distance to city center, vegetation and so on) on the definition of a particular spatial pattern for this particular outbreak in Tartagal.

To identify "hot spot" areas of the whole outbreak in Tartagal, a DF incidence map was created by accumulating the number of cases per each 3 × 3 blocks during the epidemic The raster layer was built up by assigning to each pixel a case density, equal to the number of cases per unit area. To build the predictive map, a macro-habitat conditions database was created, based on LandSat 5 TM satellite image (acquired on January 2004, path 230/row 76) and expressed as a set of raster images or layers. A synthetic multi-band image was generated including the following 13 raster layers: 1, distance to main streets and roads; 2, distances to river; 3, distance to vegetation; 4, tasselled cap brightness; 5, tasselled cap greenness; 6, tasselled cap wetness, and 7 to 13, LandSat geo-reference bands 1–7. The layers 1–3, defined as "distance to .." are calculated with the function "buffer" of the GIS software ENVI 4.1. The elements considered in the landscape (roads, rivers and vegetation) were identified directly from the image using visual interpretation and the maximum likelihood classification. The layers 4, 5 and 6 are the tasselled cap vegetation index factors: brightness, greenness, and third (Crist and Kauth, 1986; Crist and Cicone, 1984). These layers obtained by specific linear combination of the original LandSat 5TM bands, represents the "soil brightness index" (like a panchromatic image), the "green vegetation index" and the "third component" related to soil features, including moisture status (water or soil with high humidity). In our case this components were obtained directly using ENVI software. Finally, LandSat bands 1 to 7 were included to test if the data captured directly by the sensors directly represents environmental parameters associated with the DF outbreak spatial patterns. For each layer, the relation with the "case map" was estimated and the threshold

Table 1
Suspected, probable and confirmed dengue fever cases reported from the city of Tartagal between 24th of January and 11th of May 2004, and included in the analysis

Suspected DF[a] cases without laboratory tests	226	46.41%
DF cases submitted to laboratory tests	261	53.59%
Total Number of Dengue Fever suspected cases	487	100.00%
DF cases positive for IgG[b] and/or IgM	164	62.84%
DF cases positive for Den-3 IgG and/or IgM	*156*	59.77%
DF cases confirmed by viral isolation on C6/36 cells and/or PCR	5	1.92%
Suspected cases found negative or indeterminate	92	35.25%
Total	261	100.00%

[a] DF = dengue fever.
[b] Fourfold or greater rise in reciproqual IgG.

of each layer were defined using visual examination of the "hot spots", basic knowledge on vector ecology and some understanding of the layer significance in the disease outbreak. A decision tree kind algorithm was built (e.g., IF [edification LT (less than) XX] AND [distance to roads GT (greater than) XXX] and [greenness GT (greater than) 0.1], then the risk is medium), and the correlation between modelled and real data was calculated with the correlate function of the ENVI Software.

3. Results

3.1. Laboratory tests on serum samples

The 2004 dengue outbreak in Tartagal started with the report of a suspected DF case on the 24th of January 2004. Among the 487 reported suspected DF cases, laboratory investigations including serologic tests, viral isolation and PCR on serum samples were performed for 261 cases (53.59%) (Table 1). Only five DF cases were confirmed by viral isolation and/or PCR and the DEN-3 viruses were isolated. The serum of 164 cases (62.8%) was found positive for dengue virus with 156 cases confirmed as DEN-3 cases (*Instituto Nacional de Enfermedades Virales Humanas de Pergamino*, Argentina), and the serum of 92 cases (37.2%) were found negative (or indeterminate).

3.2. Epidemic description

The Argentinean Ministry of Health reported 1319 suspected DF cases in Salta province in 2004, and a total of 1354 DF cases in Argentina (last case reported on 11th May 2004). During the 109 days of the epidemic, 487

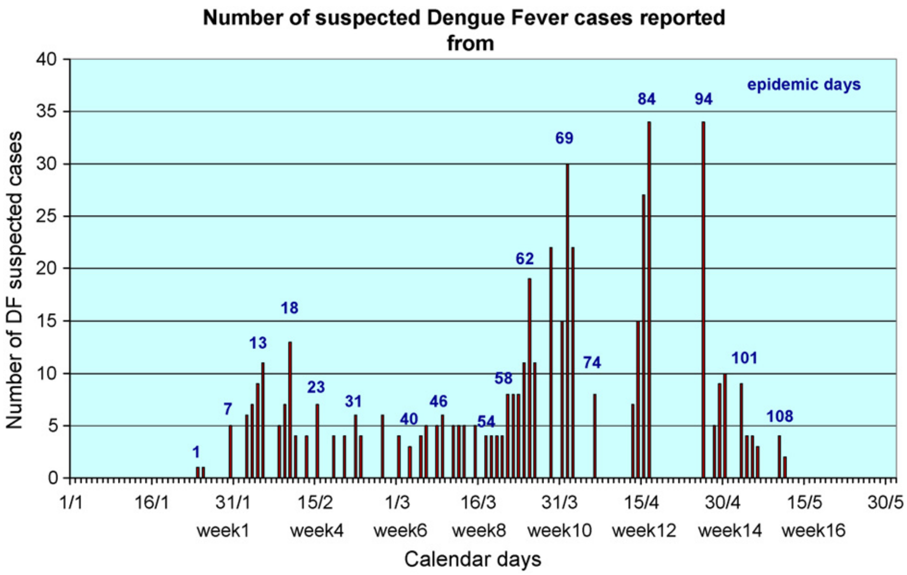

Fig. 2. Number of suspected Dengue Fever cases reported from Tartagal during the 2004 epidemic (24/01/04–11/05/04).

suspected DF cases spread throughout the population affecting 0.76% of the total population. With its origin in Pichanal city, in Salta province, the 2003–2004 DF outbreak spread along the national route number 34, due to the intensive transit of people between the towns of Embarcación, Oran, Tartagal and Salvador Mazza. The epidemic started on 24th January and ended on 11th May 2004 (Fig. 2). Approximately 49% of the cases occurred between Weeks 9 and 12, DF cases were not reported daily and the maximum time interval of no report of cases was a 9-days period including Week 13. The age distribution of the DF cases was different from the population age distribution (Fig. 3) and shows the highest incidence over 15 to 29 years old group (34%) and a lower incidence on population younger than 14 (24%) and older than 45 (14%). The dengue epidemic in Tartagal spread rapidly in all the city during the first weeks and the wide spatial DF distribution was conserved during the peak of the epidemic, at Weeks 14 to 16 (Fig. 4). A DF incidence map was built from the cumulative number of cases during the entire epidemic, and confirmed that DF cases were spreading all around the city showing a hot spot in the east side, out of the urban center (Fig. 5). This apparent cluster was due to a notification effect in the indigenous village, where spatial resolution of cases was lower, and all cases were reported from a single block that corresponded to a greater distribution area without cadastral organization. Once health services were notified of the

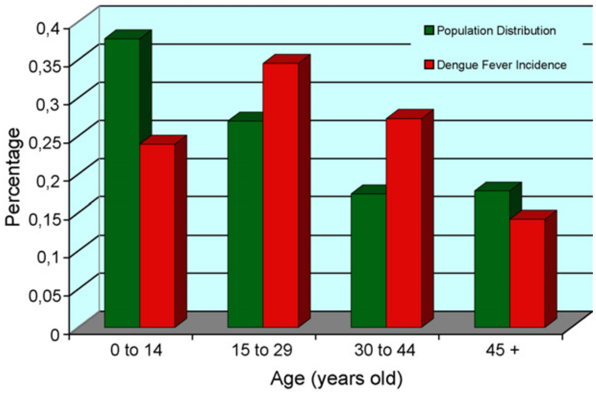

Fig. 3. Incidence per age distribution of the dengue cases during the 2004 dengue outbreak in Tartagal and population age structure.

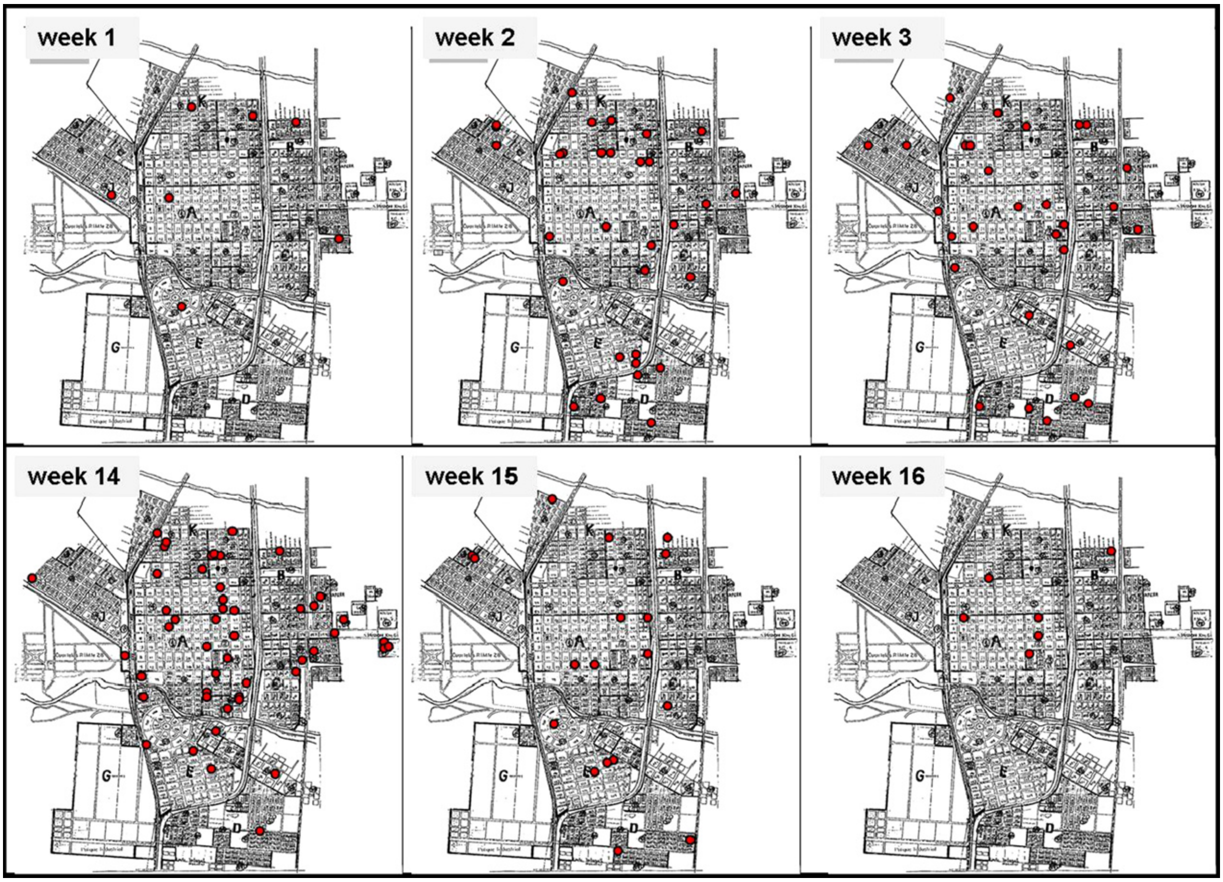

Fig. 4. Block location of suspected dengue cases for Weeks 1 to 3, and Weeks 14 to 16 in the city of Tartagal during the 2004 dengue outbreak.

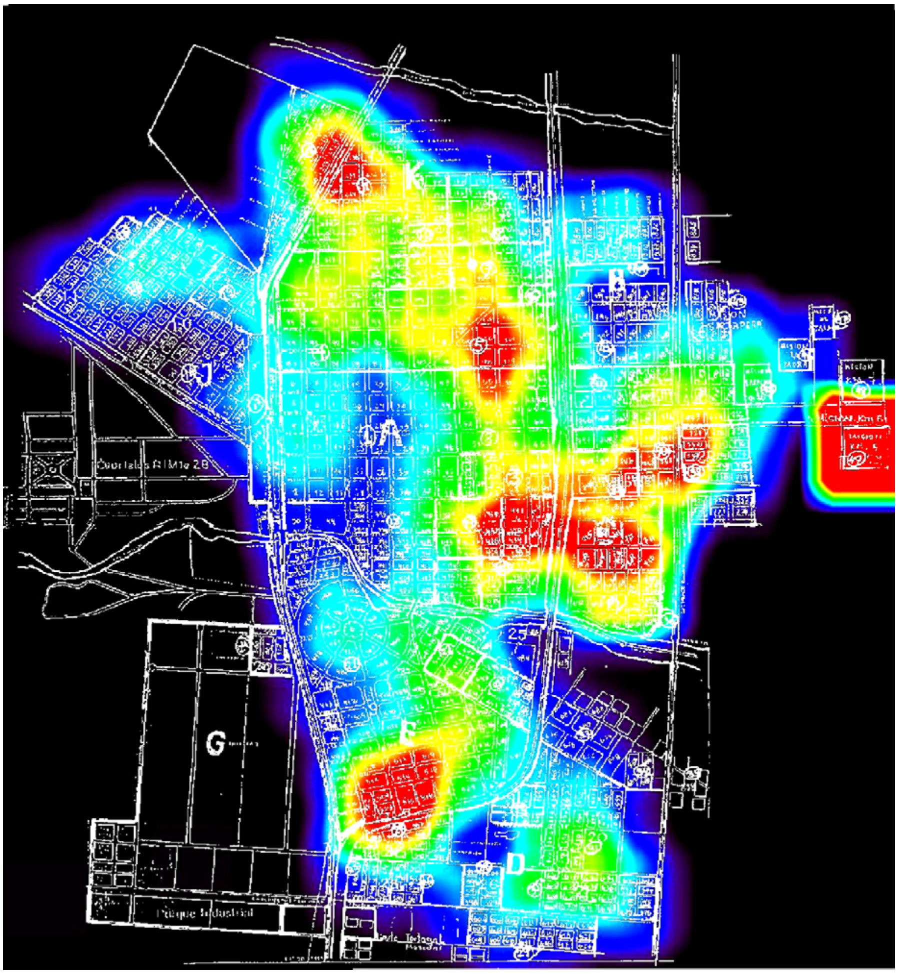

Fig. 5. Incidence map showing the cumulative number of dengue cases for the 109 epidemic days of the 2004 dengue outbreak in the city of Tartagal expressed in 3 × 3 blocks areas. The red areas represent blocks with high density of cases and the black areas blocks with no cases.

outbreak in the village, a faster expansion of the disease was observed compared to the disease expansion in urban areas.

3.3. *Space–time analysis of the dynamics of the epidemic*

The data from the 487 DF cases were considered in the analysis, and the space–time distances distribution between the suspected DF cases show a non-random pattern (Figs. 6 and 7). The distribution of the DF cases for each pair of distances (Fig. 8) showed the existence of three spatio–temporal clusters. The first cluster (top left in Fig. 8) was found for 1 day and 100 m. The second cluster (center left of Fig. 8) is much more important and appeared at Days 1 to 3, and between 500 and 2800 m. Finally, the third cluster (center of Fig. 8) was found at 12 to 15, and between 700 and 2800 m. The Fourier harmonic analysis of time distances between-cases (in an amplitude versus time plot) showed that the two more important peaks were at approximately 3 days and at Days 10 to 14 (Fig. 9). On the other hand, the fast Fourier transform of the between-cases space distance does not show any peak and is consistent with Fig. 8, where no cyclic pattern in the distance distribution is observed.

3.4. *Predictive map model*

The spatial patterns and clusters were found to be related to the following set of indicators: distances to rivers, distance to vegetation, tasselled cap brightness, tasselled cap greenness, tasselled cap wetness and LandSat band 1. Similarities of actual (Fig. 5) and predictive map (Fig. 10) obtained by the model were quantified for model goodness by the linear Pearson correlation coefficient (ENVI software correlate function) between

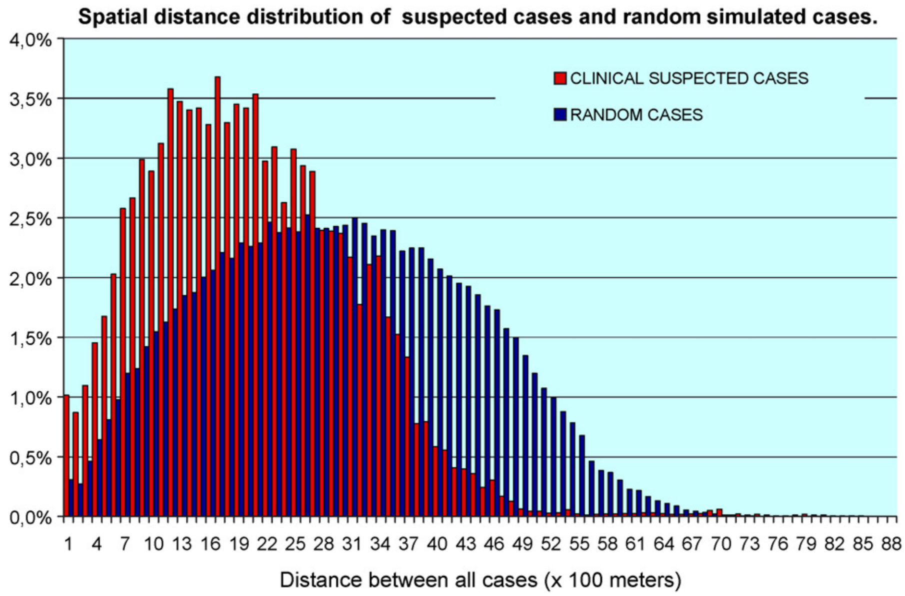

Fig. 6. Distributions of distances in the space of the dengue fever suspected cases and randomly simulated cases.

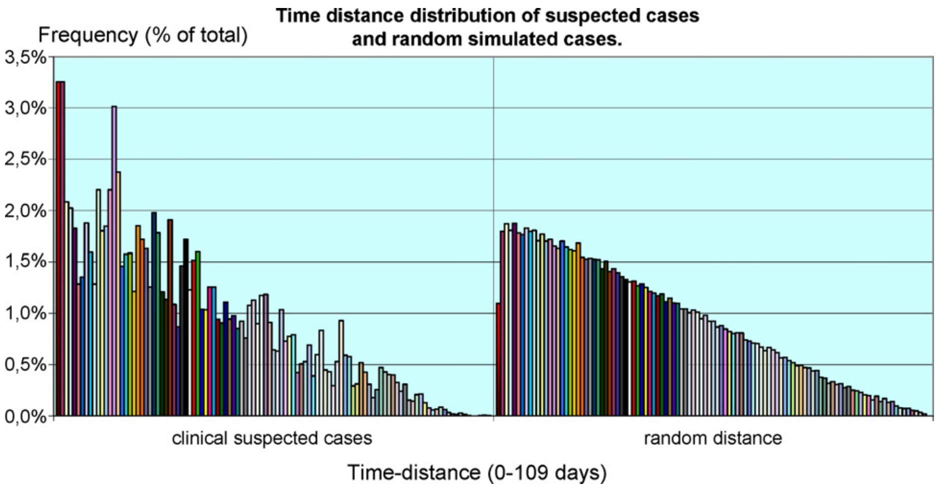

Fig. 7. Distributions of distances in the time of the dengue Fever suspected cases and randomly simulated cases.

registered incidence and predicted incidence for each group of 3 × 3 blocks area and resulted in a value of 0.68. In addition, the fit between modeled and real data was estimated using a continual arbitrary transect around the city passing alternatively over high and low incidence zones. The values of both maps showed very similar patterns with 80% of correlation (Fig. 11) between real and simulated incidence of DF cases.

4. Discussion

To analyze the dynamic patterns of the 2004 DF outbreak in Tartagal, we located all DF cases in space and time by determining their home block address and obtaining the date of onset of symptoms. Taking into account that incidence of DF is greater than expected in age group 15 to 45 years old and lower in population with less mobility like younger than 14 and older than 45 years old, a DF virus transmission out of home may be suspected. However, an underreporting in older and younger persons, the lower mosquito biting rates of children, the prior immunity to dengue in older individuals, and the mobility in young adults bringing them into contact with "hot spot" neighbourhoods may also account for the report of much of the DF cases in the age group 15 to 45. Furthermore, several studies confirmed that dengue

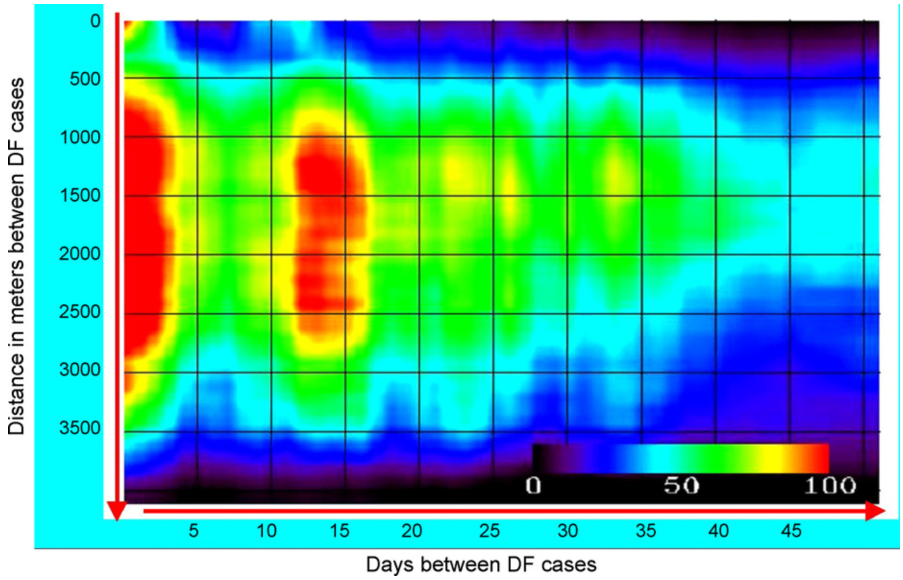

Fig. 8. Graphical representation of the number of suspected cases for each pair of distances in days and meters, with clusters of cases (vertical colored lines) indicating an apparent temporal periodicity, and apparent spatial breaks (horizontal color lines). The distribution of the DF cases for each pair of distances within the 487 dengue fever cases is represented by the colors, from 0 for no pair in purple to 100 pairs in red.

risk exposure is greater at home because of endophilic habits of *Ae. aegypti* (Rodhain, 1996; Diarrassouba and Dossou-Yovo, 1997; Chadee and Martinez, 2000), and clinical symptoms may also be less reported in young people because of a better recovery (Kourí et al., 1986). Consequently, we chose the residential block address as the best way to analyze the spatio–temporal patterns of the outbreak dynamics. Although the definition of time location is simple to deal with, the space location scale chosen introduce an error of ± 100 m due to the different location of homes in the same block and the fact that each position is inaccurately considered to be in the center of the block. Several studies in others countries (Thailand, Puerto-Rico and Peru) indicate that dengue transmission is spreading into focal points in the neighborhoods, with possibly more than one focal point in a block of houses. This pattern is possibly related to the biting behavior of *Ae. aegypti* (Scott et al., 2000).

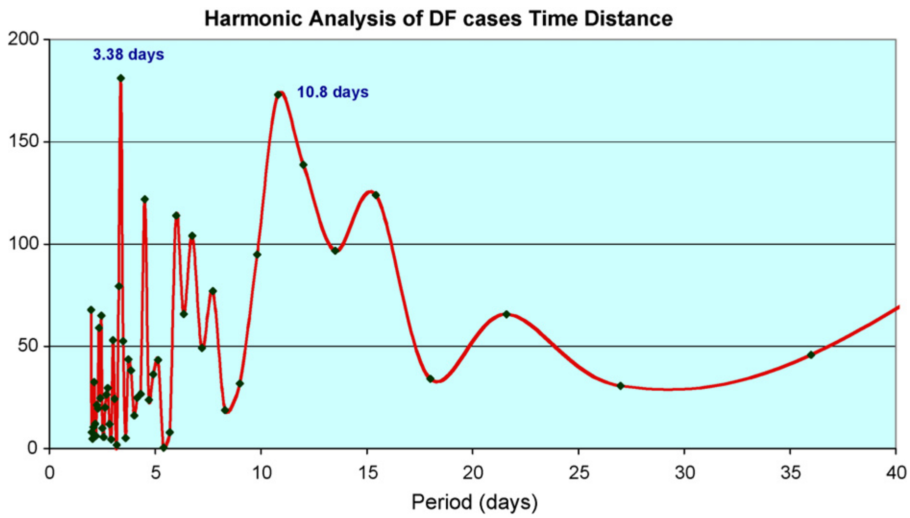

Fig. 9. Fourier harmonic analysis of time distances frequencies between suspected dengue cases. The dots with higher amplitude show the two main period peaks.

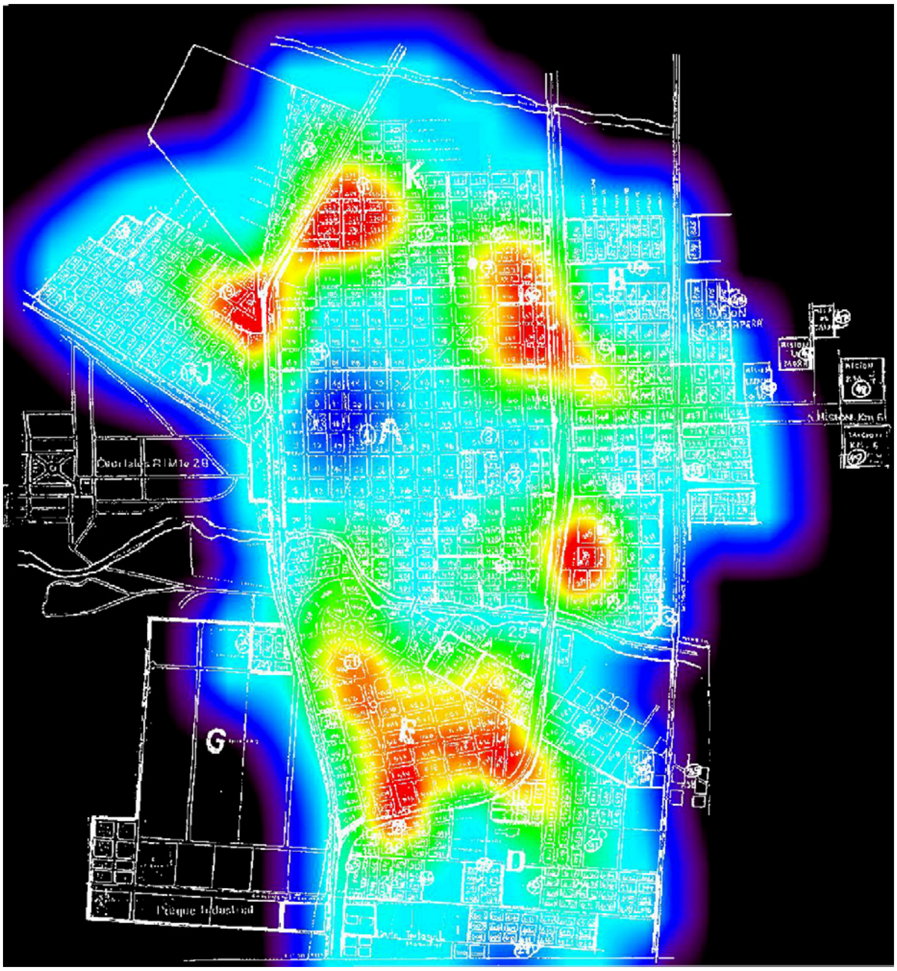

Fig. 10. Incidence map of the simulated dengue cases generated by the environmental prediction model. The red areas represent blocks with high density of cases and the black areas represent blocks with no cases.

However, it was impossible in our spatial analysis to consider each DF case address (also for ethical reasons) and the allocation of a DF case to one block was the best option.

The space–time analysis showed two clusters (Fig. 8). The possible cause of the first cluster of 1 day and 100 m may correspond to one infected female mosquito biting several people the same day (to complete his blood-meal), but without further propagation of the disease, maybe because of chemical blocking actions. The second cluster (Days 1 to 3, 500 to 2800 m) may correspond to the extension of the disease due to several infected mosquitoes, and the 3 days duration of the cluster may be related to the mosquito vector *Ae. aegypti* field survival once infected. With an Extrinsic Incubation Period (EIP) of about 10 to 12 days, plus approximately 3 days of infected life, a total of 13 to 15 days field survival seems realistic and compatible with the dengue transmission. The third cluster (Days 12 to 15, 700 to 2,800 m) could be the second epidemic wave appearing after the EIP of the second generation of infected mosquitoes. Again, this cluster has a duration of 3 days that agrees with the 15 days survival described before. The same distance of both clusters 2 and 3 is very interesting and could be the extension of the epidemic distribution, in the environmental conditions of Tartagal. In reference to the harmonic analysis, the first peak at approximately 3 days could correspond to the infected mosquito field survival (or/and gonotrophic cycle). The second peak at Days 10 to 14 could correspond to the extrinsic incubation period (EIP) for dengue viruses. The periodicity pattern observed of 3.28 and 10.8 days cases-time distance is consistent with patterns of transmission correlating with intrinsic vector biology. For the first time, and without heavy entomological studies, a mean survival duration of the females of *Ae. aegypti* could be estimated in the

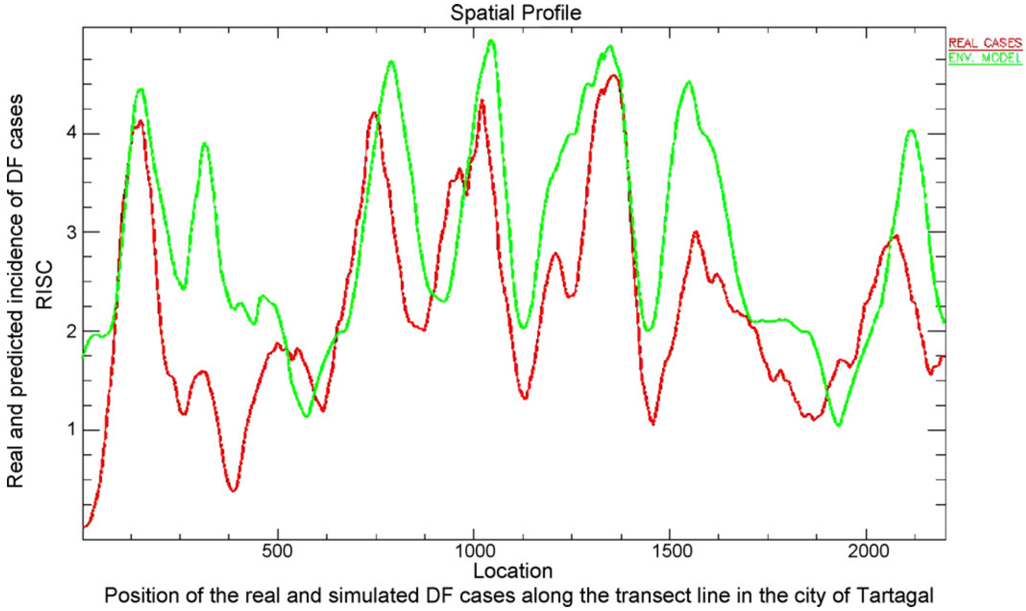

Fig. 11. Cumulative dengue cases incidence with real cases (red line) and simulated cases (green line) obtained from an arbitrary transect around the city of Tartagal.

field, with a value of 15 days corresponding to previously described estimates (Muir and Kay, 1998; Harrington et al., 2001). Moreover, the 11 days peak fit in the 10 to 14 days extrinsic dengue virus incubation period usually found at the mean summer temperatures reported in Tartagal, although longer periods can be observed with lower temperatures (Watts et al., 1987). Another important result was the extension of the epidemic with this 500 to 2800 m range. If this range is confirmed by other studies and appears to be general for Tartagal conditions, it could be used in the determination of the extension of the control activities at the very first start of the epidemic, to avoid spreading of the cases.

The simultaneous appearance of dengue cases throughout Tartagal city may have several probable explanations. First, the pattern may be due to delayed response of the dengue surveillance system. Second, people movements from Bolivia or neighboring infected cities could introduce dengue virus into the community in many places at the beginning of the outbreak and spread the virus to houses infested with *Ae. aegypti*. In spite of *Ae. aegypti* capacity to move over hundreds of meters (Reiter et al., 1995), barriers between houses and natural neighborhood barriers indicate that mosquito self-migration is not the origin of DF dispersion within the city of Tartagal. On another hand, the fast expansion and the great incidence of dengue within Amerindian colonies may be due to their housing allowing abundant development of *Ae. aegypti* with the existence of an important source of mosquitoes in the main potable water resource, used daily by the inhabitants (Personal communication from Hector Janùtolo, *Coordinación Nacional de Control de Vectores*, Tartagal, Salta, Argentina).

Vector borne diseases surveillance programs require precise and fast case location with an efficient coordination between ministries of health (for nations and provinces) and health serving institutions (hospitals, laboratories, vector control and research). Increasing satellite-based information is now available, both in quality and in quantity, and has been proved useful in generating risk maps based on spatial models. However, the use of remote sensing for dynamic spatial modeling remains linked to large-scale factors, that can explain some, but not all elements of the outbreak behavior, and the evaluation of such models can only be improved through collaborative studies among epidemiologist, ecologist and health professionals (Ostfeld et al., 2005). The macro-level factors most relevant with dengue transmission in the model presented in this paper, such as, for example, the rivers' nearness or the tasselled-cap wetness are probably linked to the ecology of *Ae. aegypti*, but we need a more precise analysis of each factor alone to better understand this relationship. Furthermore, the usefulness of such predictive map must be confirmed with the study of medium-scale and micro-scales parameters, and the prevention feasibility for the next epidemic wave (Hay et al., 2002). The results presented herein enhances the potential use of RS/GIS in epidemic surveillance and control strategy of dengue, and emphasizes the need to generalize this kind of study to others outbreaks events, feasible only if a precise geo-referencing system is available for each community. The methodology and tools developed herein could be of great help to describe latitudinal time cycles and to simulate the outbreak speed in certain areas where no field data are available. In addition, the techniques developed for modelling the spatial patterns of a dengue outbreak have some potential use for other countries. The remote sensing data can now be found for most countries and it would be very interesting to see if the parameters chosen in this study are the same (or not) for other regions, to investigate the difference and compare the results of the predictive map. The technique and model could also be extrapolated to other diseases. However, the extrapolation is limited by the available data, the surveillance system, the local facilities, and the feasibility of specific studies to complement the remote sensing results.

Nowadays in Northern Argentina, an efficient dengue surveillance program is essential to optimize the efforts of the different health programs and health stakeholders. The multi-institutional work presented in this paper represents a first step to implement daily GIS dengue maps of incidence evolution and to develop prediction models based on environmental and epidemiological data. These tools could help decision-makers to improve health system responses and prevention measures related to vector control.

Acknowledgments

We want to thank the *Comissión Nacional de Actividades Espaciales* (Argentina) for its technological and human support, and the *Ministerio de Salud de la Nación* (Argentina) for all the valuable data provided, as well as Mr. Hector Janútolo from the *Coordinación Nacional de Control de Vectores*, Tartagal, Argentina, for his work in obtaining the cases localization and comments about his field experience. This work is in the frame of the international cooperation program MATE, between the *Comission Nacional de Actividades Espaciales* (CONAE) of Argentina with the coordination of Cs. Felix Menicocci and the Centre national d'études spatiales (CNES) from France, with the coordination of Dr Murielle Lafaye. This work was supported by the *Comission Nacional de Actividades Espaciales* (CONAE) of Argentina, the *Ministerio de Salud* of Argentina and the French *Centre national d'études spatiales* (CNES).

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