Spatial correlations of population and ecological factors with distribution of visceral leishmaniasis cases in southwestern Iran

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ABSTRACT

Background & objectives: Leishmaniasis as a dynamic disease may be markedly influenced by demographic and ecological factors. A geospatial information system study was developed to determine the distribution of visceral leishmaniasis (VL) cases in relation to population, climatic and environmental factors in Fars province, southwest of Iran.

Methods: The dwelling addresses of 217 VL patients were obtained from hospital files. A hazard map produced by unifying buffers (5 km) around nomads travel routes (NTR) was developed to survey the effect of close proximity to NTR on the distribution of VL. Mean annual rainfall (MAR), mean annual temperature (MAT), four months temperature mean (T4), elevation, slope and landcover were climatic and environmental factors that have been analysed. Finally, data of dwelling foci were extracted from maps and analysed using logistic regression models.

Results: Close proximity to NTR was the most important factor influenced on the disease distribution. Climatic factors were in second rank. Among them, temperature especially T4 is the most effective variable and rainfall was also shown to be another effective climatic agent. Most cases of VL were reported from temperate and semiarid areas in western and central regions while arid condition was a confined factor. The environmental factor of landcovers including urban, dry farm and thin forest regions was revealed as the third rank effective factor. Altitude importance was only shown when its effect was studied independently from other factors.

Interpretation & conclusion: These findings present the distribution of VL in Fars province is influenced by combination of ecological and nomads demographical variables although closeness to NTR and nomads role in distribution and continuance of kala-azar are the most important factors.

Key words Fars; GIS; Iran; landcover; nomads; rainfall; temperature; visceral leishmaniasis

INTRODUCTION

Leishmaniasis is a protozoan parasitic disease caused by the *Leishmania* genus and transmitted by sandfly bites. This disease is endemic in 98 countries and territories over four continents and has resulted in 2,357,000 disability adjusted life years (DALYs). Its visceral form, known as kala-azar, is a major public health problem in endemic countries and is almost fatal, if left untreated, with 20,000 to 40,000 deaths annually^{1, 2}. The main endemic foci of visceral leishmaniasis (VL) in Iran are: the northwest region including Ardabil and eastern Azerbaijan, and the southwest region including Fars and the neighbouring provinces of Bushehr, Kohkilouyeh and Booyerahmad³⁻¹⁰.

Fars is one of the largest and most populated provinces in southern Iran. *Leishmania infantum* is the principle causative agent of Mediterranean type zoonotic visceral leishmaniasis (ZVL), which occurs in this province. This parasite circles between phlebotomine vectors, dog reservoirs and humans as accidental hosts. Human infection is dependent on the ecological relation between human activity and reservoir systems¹¹. Leishmaniases as vector-borne diseases are dynamic, and climatic and environmental conditions, as well as demographic and human activity factors contribute to the distribution and landscape of the disease, especially in temperate zones¹². The Fars area encompasses various climatic, geographic and population properties, some of which may be contributory to the endemicity and continuance of VL in this region. In recent years, the identification and survey of the effectiveness of these probable risk factors and prediction of trends of disease distribution has been conducted by remote sensing (RS) and geospatial information systems (GIS) approaches, which have been increasingly used in public health studies such as those for vector-borne diseases¹³.

A GIS study was, therefore, designed at a macro-epidemiological level and the latitudes and longitudes of the villages or cities patients were referred and recorded as a point vector layer. Climatic factors such as temperature, rainfall, elevation, and slope were calculated for each point, and demographic properties such as the routes of immigration for migratory populations were considered within the other calculations. Finally, comparison was carried out between infected and clean locations. The only GISbased study to be carried out, was conducted in northwest Iran on the effect of climatic factors on VL and it demonstrated that the number of days at or below freezing point in a year was significantly related to the number of dogs with high serological titre¹⁴. To our knowledge, this study is the first comprehensive survey of VL in the southwest foci in Iran using GIS technology although the complexity of nomadic immigration and spectrum of weather conditions in this region makes this model as a unique experience. The intention of this study was to clarify the effects of human population, and climatic and environmental factors on the distribution of VL in this region.

MATERIAL & METHODS

Study area

Fars province is the fifth largest province, covering an area of 122,608 km² and located between latitudes 27° 03' and 31° 40' and longitudes 50° 36' and 55° 35' in the southwest of Iran. The region contains a variety of landscapes from dense forests to bare lands and has an elevation of approximately 115 to 3115 m above sea level, while the Zagros mountain chain extends from the north to the south and the mountains cover 70% of the province. The weather also varies in different regions. Based on isohydral and isothermal maps, Fars province can be divided into different regions based on the different weather conditions presented in Table 1. The population structure of this province consists of those dwellings in

 Table 1. The division of different regions of Fars province

 based on weather conditions

| Weather condition | Region | | | | |
|-------------------------|-----------------------------|--|--|--|--|
| Warm and arid | Southeast, south, southwest | | | | |
| Temperate and semi-arid | Middle, west | | | | |
| Temperate and arid | East | | | | |
| Cold and arid | Northeast | | | | |
| Cold and semi-arid | North | | | | |
| Cold and wet | Northwest | | | | |
| | | | | | |

the villages and cities and migratory human populations (nomads). Nomads are populations belonging to different tribes who spend their life herding and travel from their summer quarters (Yailaq) to winter quarters (Qishlag) through defined routes. As part of their way of life they are in close contact with dogs and the breeding places of sandflies, which are significant factors in the VL circle. Fars is the main VL endemic province in southwest Iran and VL patients have been reported from different regions of this province.

Data collection

VL is diagnosed and treated in specialised centres. Although in some cities around the province, specialists provide care to the patients, a referral hospital in Shiraz (Namazi Hospital), the capital of the province, is the main centre with the most sophisticated diagnostic tools. Therefore, almost all the suspected cases are referred to Namazi Hospital at least once. A few cases have also been referred to the Paediatric Centre of the Ali-Asghar Hospital in the capital of the province.

Data from 217 patients admitted and treated in these hospitals from 2000 to 2012 were gathered. These were clinically diagnosed as kala-azar cases and confirmed by one or multiple methods such as bone marrow or spleen aspiration microscopic examination, rk-39 strip test, indirect fluorescent antibody test (IFAT >1/128 accepted as positive result) and KAtex serological tests and PCR, with bone marrow aspiration and IFAT being the most frequently used.

The precise residential address of each patient was recorded from the patients' hospital files. The data enabled us to determine their city or village. The validity of hospital records was reconfirmed when we randomly called the phone numbers recorded with the address of each patient's residence. This sometimes varied for the centre of province, because some patients were referred from distant villages and had given their relatives' addresses in Shiraz rather than their own village addresses. The data were corrected. The nomads also gave their addresses of nearest villages or cities to their original dwelling places and we accepted these addresses because the distances inbetween were short and, therefore, would not influence the climatic analysis.

Geospatial data

The patients' residences were recorded and determined on the Fars province shape file map which included counties, rural districts, villages, and cities based on the latitudes and longitudes of the villages or cities from which the VL patients were referred. The number of patients in each village or city was imported into the layer attribute field and analysed for each rural district and county. Each province contains counties and each county is divided into rural districts.

Digital elevation model (DEM) and landcover maps were retrieved from the Department of Natural Resources of Fars province. Landcover is a vector layer and shows different features covered within Fars province. A slope raster map was produced, based on DEM by calculating the maximum rate of change in value between each cell and its neighbours by using spatial analyst tool. Monthly and annual temperatures from 24 synoptic meteorology stations and the annual rainfall from 43 rainfall assessment stations for the years were obtained from the Fars Province Weather Bureau. Mean annual temperature (MAT) and mean annual rainfall (MAR) were calculated based on annual temperature and annual rainfall of the studied years, respectively. ArcGIS version 9.3 (http:// www.esri.com/arcgis) was used to analyse geospatial and related climatic and demographic information. After checking different interpolation methods, the annual isohydral and isothermal rasters were developed using the tension based Spline interpolation model with a resolution grid of 2×2 km for Fars province.

An investigation of hospital records revealed that mostly the VL cases were found between February and May in different years. With respect to the incubation period of kala-azar, which is usually reported to be between 2 and 6 months after a sandfly bite¹⁵, the presumed time of parasite transmission by sandflies was considered as corresponding to mid-August to mid-December when the weather is temperate and suitable for sandfly activities. Therefore, an isothermal raster for a four month period (T4 variable) from mid-August to mid-December was developed.

The Fars province shape file map (including villages and cities points) was extracted with all raster maps, including annual rainfall, annual temperature, temperatures covering four months, digital elevation model and slope. The geometric intersection of the layer obtained from the extraction of the above mentioned layers and landcover polygonal shape file was computed by an identity tool to produce the final layer in which each point presented properties of all overlapped identity features from the above mentioned raster and vector layers. The attribute of this layer was converted to excel format for statistical analysis.

Hazard map

The nomads travel routes (NTR) vector map was retrieved from Fars Nomads Affairs Administration. A hazard map produced by unifying the buffers (5 km) was developed around the ways in which nomadic immigrants travel from summer quarters (Yailaq) to winter quarters (Qishlag) and *vice versa* to survey the effect of nomads on VL occurrence.

Statistical analysis

Having described the spatial distribution of cases and their demographic variables, we explored the link between the risk of disease and geographical features such as landcover and meteorological factors. The effect of close proximity to nomadic migration routes on VL occurrence was also determined. For these analyses, data of dwelling foci were extracted from maps and analysed using logistic regression models. The analyses were carried out using SPSS version 16.

RESULTS

Distribution of VL in the province

VL patients were reported in different regions, including 141 points in Fars province. The majority of the cases were from the middle and western regions of the province (predominantly Kazeroon and Shiraz counties), although a major focus was also in the southeast (Darab county). Some (four) counties in the southwest and northeast of the province were found to be clean counties, because no VL patient was reported from these counties in our study. Among the rural districts, most VL cases were reported from six rural districts, five of which belonged to the middle and western regions and one belonged to the southeast focus. Although most of the cases were reported from villages, 16 points being the maximum number of VL cases, 10 points were city-based (Fig. 1). The point with the highest level of prevalence was Sarmashhad, a village in the western region of Fars province.

Effect of hazard map on VL distribution

A survey of the close proximity of VL reported points to nomadic travel routes was carried out in all the 141 villages and cities from which VL was reported, where 116 rural and urban locations (82.2%) were covered by the hazard map and 191 (88%) out of 217 cases were found within 5 km buffer zone. Based on our calculation, 25 of the 3569 locations out of the buffer zone reported at least one case (0.7%), while 116 of the 4601 locations within the buffer zone reported at least one case (2.5%). The odds ratio (OR) of locations within the buffer zone reporting at least one case was 3.7 (2.3–5.9), which was highly significant and showed that the buffer zone obviously increases the chance of disease significantly (p < 0.0001). Furthermore, a study of the map which in-



Fig. 1: The frequency of VL patients in counties and in rural districts and points with most cases.

cluded both patient reported points and NTR vector layers, illustrated the accumulation of these points corresponded to where nomadic travel routes were crossed, or accumulated and a small branch of one tribe's travel route unified with the main route like the crossing points of Arab tribe travel routes in the southeast, or where different tribes' travel routes passed or crossed as occurred in the central and western regions (Fig. 2). In the map, five hot points were illustrated at which VL reported points accumulate on the cross roads of nomadic journey routes.

Other factors including climatic and environmental agents

Geospatial, and climatic and geographic analysis based on DEM, slope, only isohydral and isothermal raster maps in Figs. 3 and 4 showed that the different points where from patients were reported, have different climatic conditions. The MAT for the mentioned points varies with a range from 13 to 26°C. The MAR differs from 140 to 955 mm. The minimum and maximum elevation, and slope were 203 and 2996 m and, 0 and 34 degrees respectively. The four months temperature mean also differed from 13 to 25°C among different polluted points. Table 2





shows the situation of different Fars province counties with respect to climatic and geodemographic conditions and the number of VL cases reported from there.

The various landcovers have expanded in Fars province. The frequency of polluted points, as well as all existing points in different landcovers are shown in Table 3. The majority of cases were reported from irrigated farms and gardens, thin rangeland, urban sites (regions covering a minimum of 25 ha of human residential areas based on primary remote sensing data), and sparse forests. Points with reported cases of VL were observed more often in urban, dry farm, and sparse forest areas in comparison to villages and cities (points) in the same areas (Fig. 5). There were no cities or villages located in the landcovers of shrub land, swamps and cane-brakes in this province.

The logistic regression for single variable model which showed temperature [including both T4 and MAR variables with higher effectiveness (odds ratio) for T4] and elevation had significant effect on occurrence of dis-



Fig. 3: Isohydral model raster map of Fars province. The polluted points are illustrated.





Fig. 4: Isothermal model raster map of Fars province. The polluted points are illustrated.



Fig. 6: The presumed band surrounds most cases and NTRs in Fars province.

| Region | County | Patient frequency | T4 ^{Ave} | MAT ^{Ave} | MAR ^{Ave} | ELV ^{Ave} | SlopeAve | NTR length (km) |
|-----------|-------------|----------------------|-------------------|--------------------|--------------------|--------------------|----------|--------------------|
| Middle | Shiraz | 40 | 18 71 | 19.7 | 315 | 1682 | 3.81 | 1326.4 |
| Windele | Firoozabad | 13 | 21.65 | 21.98 | 294 | 1456 | 5.09 | 382.3 |
| | Ghirokarzin | 10 | 21.03 | 21.56 | 276 | 752 | 5.01 | 215.3 |
| | Jahrom | 10 | 20.25 | 20.42 | 268 | 1233 | 5.15 | 452 |
| | Fasa | 7 | 18.99 | 19.44 | 250 | 1432 | 2.91 | 151.4 |
| | Marvdasht | 7 | 16.41 | 16.99 | 351 | 1673 | 5.68 | 383.3 |
| West | Kazeroon | 50 | 22.39 | 22.42 | 418 | 904 | 6.75 | 485.6 |
| | Farashband | 8 | 23.9 | 24.21 | 292 | 766 | 4.22 | 268.2 |
| Northwest | Sepidan | 5 | 16.45 | 16.43 | 550 | 1965 | 6.41 | 511.7 |
| | Mamassani | 11 | 17.35 | 16.9 | 644 | 1214 | 10.15 | 496 |
| North | Abadeh | 1 | 13.42 | 13.89 | 207 | 2135 | 2.43 | 5.2 |
| | Eghlid | 4 | 13.56 | 13.79 | 480 | 2297 | 2.48 | 724.6 |
| Northeast | Bavanat | 2 | 15.01 | 15.36 | 179 | 2240 | 4.66 | 199.6 |
| | Pasargad | 0 | 16.72 | 16.88 | 229 | 1856 | 4.41 | 157.7 |
| | Khorambid | 0 | 12.28 | 11.72 | 193 | 2312 | 2.72 | 0 |
| East | Arsanjan | 2 | 18.21 | 18.48 | 192 | 1649 | 5.3 | 129.6 |
| | Neyriz | 2 | 20.22 | 20.44 | 174 | 1745 | 3.08 | 144.2 |
| | Estahban | 2 | 17.8 | 18.4 | 222 | 1643 | 4.12 | 58.1 |
| Southwest | Mohr | 0 | 24.86 | 24.97 | 187 | 463 | 3.67 | 27.7 |
| | Lamerd | 0 | 25.04 | 24.74 | 173 | 452 | 3.04 | 43.1 |
| | Khonj | 5 | 22.86 | 22.97 | 230 | 622 | 3.76 | 250.2 |
| South | Larestan | 6 | 23.25 | 23.77 | 175 | 809 | 3.72 | 345 |

Table 2. Climatic and geodemographic conditions and the number of reported VL cases from different Fars counties

T4^{Ave}— County four months temperature mean average; MAT^{Ave}— County mean annual temperature average; MAR^{Ave}— County mean annual rainfall average; ELV^{Ave}— County elevation average; Slope^{Ave}— County slope average; NTR length: Nomads travel routes length in each county.

23.82

24.07

183

183

23.26

23.6

| Table 3. The distribution of VL polluted points and all province |
|--|
| points in different landcovers in Fars province |

4

28

Zarrindasht

Darab

| Table 4. H | Results | of the | single | and | multiva | riate | logistic | regression |
|------------|---------|---------|--------|-------|----------|-------|------------|------------|
| | model | for cli | matic | and o | environn | nenta | al factors | S |

1062

1334

3.02

4.92

242.3

353.6

| Landcover | Polluted points per feature (%) | All points per feature (%) | Ratio |
|---------------------------|---------------------------------|----------------------------|-------|
| Urban | 14.9 | 1.3 | 11.46 |
| Dry (rainfed) farm | 4.3 | 2.1 | 2.05 |
| Sparse forest | 14.2 | 10.1 | 1.4 |
| The forth of the river | 0.7 | 0.6 | 1.17 |
| Irrigated farm & garden | 40.4 | 41.6 | 0.97 |
| Thin rangeland | 18.4 | 27 | 0.68 |
| Bare land & without cover | 1.4 | 2.1 | 0.67 |
| Semi-condensed forest | 2.2 | 4.9 | 0.45 |
| Semi-condensed rangeland | 3.5 | 8.9 | 0.39 |
| Condensed forest | 0 | 0.4 | 0 |
| Salt land and salinity | 0 | 0.4 | 0 |
| Planted forest | 0 | 0.1 | 0 |
| Water area | 0 | 0.2 | 0 |
| Condensed rangeland | 0 | 0.4 | 0 |
| Total | 100 | 100 | |

| Logistic regression | Variable | <i>p</i> -value | OR | Nagelkerke's R^2 |
|---------------------|-----------|-----------------|-------|--------------------|
| Univariate | T4 | < 0.001 | 1.121 | 0.017 |
| | MAT | < 0.001 | 1.114 | 0.016 |
| | MAR | 0.22 | 1.001 | 0.001 |
| | Elevation | < 0.001 | 0.999 | 0.014 |
| | Slope | 0.181 | 0.980 | 0.002 |
| | Landcover | 0.212 | 1.042 | 0.001 |
| Forward stepwise | T4 | < 0.001 | 1.189 | 0.033 |
| multivariate | MAR | < 0.001 | 1.003 | |
| (Step 3) | Landcover | 0.05 | 1.272 | |

Sig: The statistical significance of each factor in VL occurrence; OR: Odds ratio (exponential B), which shows the relative increase or decrease effect of each factor; T4: Four months temperature mean; MAT: Mean annual temperature; MAR: mean annual rainfall.

temperature and elevation factors were slightly higher than other aforementioned factors.

In the forward stepwise multivariate model, only T4, MAR and landcover were entered and showed significant association with disease occurrence. The influence of other variables was not significant and their effects were automatically removed. T4 is the most important

ease, where as expected, temperature and elevation revealed an inverse relation. Accordingly, both increase in temperature and decrease in elevation increased the chance of VL occurrence. But landcover, rainfall and slope had no significant effect on occurrence of the disease. Based on Nagelkerke's R-Square calculation, goodness of fit of

Southeast

factor which played a role in the model, and MAR and landcovers have a lower significance. Increase of one unit of each of the aforesaid factors increased the possibility of VL for landcover, T4 and MAR by 27, 19 and 0.3%, respectively (Table 4).

Overall, 95% of the cases occurred at locations with an altitude ranging from 477–2402 m, elevation 0.23– 23.5 degrees slope, 164–712 mm annual rainfall, and 13.6–25 mean annual temperature.

DISCUSSION

Our study targeted the role of climatic and human population factors on VL distribution. With respect to our findings, the most important factor for the distribution of VL is close proximity to nomadic travel routes. Climatic factors ranked second. Among these, temperature, especially T4 is the most effective variable, and rainfall was also shown to be another effective climatic agent. Most of the cases of VL were from temperate and semi-arid areas in the western and central regions. Arid condition was a confined factor for distribution of the disease. The environmental factor of landcovers including urban, dry farm and sparse forest regions was revealed as the third ranked effective factor for VL distribution in Fars province. The importance of altitude was only shown when its effect was studied independently from other factors.

The importance of close proximity to NTRs was wellpresented when 82% of the polluted villages and cities accumulated in a 5 km buffer around. Furthermore, accumulation of polluted villages and cities at the locations where NTRs accumulated or crossed reconfirmed the role of nomads and close proximity to NTRs. NTRs in the Fars province extend to Kohkilouyeh and Booyerahmad province in the northwest and Bushehr province in the west and southwest. Interestingly, all these regions compose the southwest endemic foci of VL in Iran. Based on the trend of distribution of VL cases in the Fars, a presumed band is conceivable, stretching from the northwest to the southwest of the province (Fig. 6) and most of the cases are accommodated within this band, which of course is concordant with the distribution of NTRs in the province. Different studies exist on the role of population immigration on the distribution and occurrence of emerging or re-emerging leishmaniasis disease^{2, 16–18}.

How nomads play this role can be explained by their life structure and style. Nomads, as a population which live by herding sheep and goats, usually own a notable number of dogs. Furthermore, immigration twice a year, with routes as long as hundreds of kilometres through different kala-azar endemic regions and through a variety of land coverage, exposes them and their dogs to the regions of sandfly breeding and activity. They also move within or near regions in which stray dogs or wild Canidae live or roam. The nomads usually have no access to good quality sanitary facilities and most probably fail to attend medical centres for health related issues. In the 20th century and today, many nomadic people have been changing their life-style and exchanging a migrating life for a life in the villages and cities. Therefore, there are people in villages and cities who are relatives of immigrating nomads and have a close relationship with them, subsequently playing a role in the maintenance of the disease in these regions. All of these high risk conditions were caused that nomads have been converted as high risk population for kala-azar which resulted in stability of VL in Iran southwest foci. Some serological studies have shown high seropositivity for antileishmanial antibodies in the nomadic population and confirm our conclusion. Mohebali et al8 reported that 1.7% of nomadic children were seropositive, compared to 0.9% of the settled population in endemic regions, which was a significant difference¹⁹.

Study of climatic factors revealed that temperature (including MAT and T4) plays a notable role after NTR effect. T4 as the most effective climatic variable, indirectly showed the effect of temperature on sandflies as vectors of *Leishmania*. This was because T4 was the result of average temperatures of months in which we anticipated that *Leishmania* transmission was actively induced by vectors. This finding showed the role of a temperate climate of late summer and autumn on the reproduction and activity of sandflies in the Fars province.

The second ranked climatic effective variable is MAR. According to our results, mostly the patients were reported from temperate and semi-arid regions, which equated to central and western counties in the Fars province. Mostly the counties and rural districts with the maximum number of cases were also within these regions and the most VL prevalent point was a village in the western region. The semi-arid regions have also been shown as important foci of VL in other studies. For instance, in Brazil, semi-arid and hot climates were presented as the highest VL occurring regions in Bahia state. Elsewhere in Kenya, all the VL cases occurred in semi-arid and arid regions^{20–21}.

Our results also showed that the regions with no cases or low VL reports are confined to warm and arid southwestern, temperate and arid eastern, and cold and arid northeastern regions of the province, all of which share a common property of being arid, whilst a wide range of temperatures was observed in these regions. So aridity is a confined factor for VL occurrence in the Fars province. Of course regions in the southeast and at southern locations are exceptional areas, which do not follow the above mentioned pattern. Salahi-Moghadam *et al*¹⁴ showed that an increase in days at or below freezing point is an effective factor for a decrease in VL occurrence in the northwestern Iran and this could also explain the effect of coldness on VL occurrence in the northeastern regions of the Fars province.

Land coverage has a less significant role in the model. This variable has been presented in different studies as an effective factor for the distribution of VL or the parasite vectors^{22–25}. Urban, dry farm and sparse forest contribute to the distribution of VL in the Fars province. A notable number of cities and villages are within the urban landcover. Furthermore, suburban regions with low social facilities and quality of life also play a role as high risk regions for VL^{16, 26}.

Dry farm lands are important with respect to agricultural activities, which may result in the provision of suitable breeding places for sandflies, and the role of sparse forest can be debated with respect to the abundance of leaf-falling trees, e.g. oak (*Quercus persica*), wild almond (*Amygdalus scoparia*), terebinth (*Pistacia terebinthus*), common fig (*Ficus carica*) and Persian juniper (*Juniperus polycarpus*), as an accumulation of their leaves produces conditions ideal for sandfly reproduction and activity, similar to what occurred in North America²⁵. Furthermore, sparse forests are the habitat for canidae family animals, e.g. foxes, wolves, and jackals, which occasionally come to neighbour farms and gardens and suburban regions seeking food.

Elevation factor decreases the chance of VL occurrence according to independent analyses, but multivariate logistic regression failed to confirm its effect. In our study, elevation had a reverse effect relative to temperature. Elnaiem *et al*²⁷ also showed altitude to be negatively correlated to VL incidence in eastern Sudan.

Overall, although climatic and environmental factors have a significant effect on how VL is distributed, close proximity to NTR is the most effective factor. The controversy of low rainfall concordant with high VL occurrence in some arid southeastern and southern counties is resolved when calculations of the length of nomadic travel routes is examined to reveal the considerable length of these routes in those counties. Furthermore, the counties with lower number of cases in arid regions also have fewer nomadic travel routes within them and three out four clean counties presented either none or the shortest length of a route between all counties (Table 2).

There are some limitations for this work also as ob-

served in many studies such as the present one. For instance, although personal data registered in the hospital records are a reliable source for determination of patients' addresses, imprecise addresses, however, or misleading data may be submitted by few patients. This can be ignored by checking the accuracy of addresses before importing to the study. Furthermore, the addition of serological or molecular epidemiological surveys could strengthen our results on the severity of VL occurrence in each focus and reconfirm the reproducibility of our results.

Considering nomadic influence as a population on VL occurrence, instructions of their dog owners and intensive control and treatment of dogs would seem to be a mandatory recommendation. Government investment on programmed medical surveillance and sanitary conditions of nomadic tribes as well as comprehensive studies on sandflies in the regions around nomadic travel routes are also highly recommended. With respect to the increasing trend of nomads, dwellings in cities and villages, the possibility of the emergence of new foci, especially in larger cities cannot be ignored. We strongly recommend targeted studies on nomadic influence on the distribution of VL in endemic countries in which populations of nomads are notable. Global warming and changes in climatic conditions can also affect the distribution of disease in this region and follow-up studies are required.

CONCLUSION

The conclusion attained by these findings on distribution of VL in the Fars province is that it is influenced by a combination of environmental and nomadic demographical variables, although close proximity to NTRs and the role of nomads in the distribution and continuance of kala-azar are the most important factors. This study has provided a foundation which serves as a guide for researchers in the management of different studies in a variety of aspects of kala-azar in this region.

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