Original Article

The Effect of Geographical and Climatic Factors on the Distribution of Phlebotomus papatasi (Diptera: Psychodidae) in Golestan Province, an Endemic Focus of Zoonotic Cutaneous Leishmaniasis in Iran, 2014

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Abstract

Background: Phlebotomus papatasi is known as the main vector of zoonotic cutaneous leishmaniasis. This study aimed to investigate the effect of geographical and bioclimatic factors on the Ph. papatasi distribution.

Methods: A total of 34 villages were selected, and sampling was performed three times using 120 sticky traps in each selected village. All the collected species were mounted and identified their species. The densities of Ph. papatasi were measured in all the villages and entered into ArcMap as a point layer. The required bioclimatic and environmental variables were extracted from the global climate database and The normalized difference vegetation index was obtained from the MODIS satellite imagery, also, all variables entered into ArcMap as raster layers, so The numerical value of each independent variable in the cell where the selected village is located in this, was extracted using spatial analyst tools and the value to point submenu. All the data were finally entered into IBM SPSS, and the relationship was examined between the number of collected Ph. papatasi and the independent variables using Spearman's correlation test.

Results: A total of 1773 specimens of Ph. papatasi were collected. The findings of this study showed that max temperature of warmest month, temperature annual range, temperature seasonality, mean diurnal range, precipitation seasonality, mean temperature of driest and warmest quarter were positively associated with the density of Ph. papatasi.

Conclusion: Air temperature and precipitation were shown as the most significant factors in the distribution of Ph. papatasi.

Keywords: Ecology; Phlebotomine sand fly; GIS

Introduction

Leishmaniasis is one of the most important vector-borne parasitic diseases and appears as a significant health problem in Iran. Cutaneous and visceral leishmaniasis are two types of the disease in Iran. The cutaneous leishmaniasis (CL) is also prevalent in two forms of anthropogenic cutaneous leishmaniasis (ACL) and zoonotic cutaneous leishmaniasis (ZCL) in the country (1). Different studies conducted in Iran showed that vectors for ACL and ZCL were Phlebotomus sergenti and Phlebotomus papatasi, respectively (1-3).

In Golestan Province as one of the most important ZCL foci in Iran (4-8), Leishmania major is the agent and wild rodents such as Rhombomys opimus and Meriones libycus are reservoir hosts of ZCL (9-11). In a wide range of similar studies conducted in the province, Ph. papatasi was shown as the main ZCL vector and the infection range of Ph. papatasi to L. major was reported as 10% (11-12). Further, various studies conducted in the province showed the CL incidence equal to 31.7 per 100,000 people. among them, the two counties of Gonbad-e Kavus and
Maraveh Tappeh located in the northeast of the province had the highest incidence rates of 153 and 117 per 100,000 people (13). During 2010–2017, 360–1766 people from all age and gender groups in the province were infected with CL annually (14). Compared to the other regions of the province, the vectors and reservoirs of the disease are more abundant in the northeastern region of the province and the disease has higher incidence. These differences could be reasons for the geographical and climatic susceptibility of the region to a higher prevalence of the disease (13, 15).

Leishmaniasis is naturally dependent on environmental factors and climate change (16), and the environment plays a significant role in the transmission of the disease (17). Due to different species of agents and vectors, environmental changes can have various effects on the transmission of leishmaniasis in different regions of the world (18). Hence, environmental factors and climate change may significantly affect the growth, development, and distribution of Ph. papatasi as the main ZCL vector. Temperature and relative humidity are known as the most significant factors associated with the distribution of Ph. papatasi (19), and the climate change that has taken place in recent years has become a critical factor in the distribution of this species (17). It is also believed that the wide distribution of this species in the nature is dependent on environmental conditions and many of these conditions are measurable (20). Therefore, in recent years, many studies have been carried out on finding effective factors in the distribution of Ph. papatasi and several factors have been considered as essential factors in the distribution of this species. In a study conducted in Golestan Province (21), slope, altitude, annual mean temperature, and the normalized difference vegetation index (NDVI) were introduced as the most significant factors in the distribution of Ph. papatasi. Another study conducted in Iran (22) also reported the mean temperature of the wettest quarter, slope, precipitation seasonality, and the precipitation of the wettest quarter as major factors associated with the distribution of this species. A study conducted in Eastern Mediterranean (23) revealed that land cover, mean temperature of coldest quarter, max temperature of warmest month, and min temperature of coldest month were the most critical factors for the distribution of Ph. papatasi. Further, in a study conducted in Libya (20), the altitude from the sea level was reported as a major factor associated with the distribution of Ph. papatasi. Given the significance of Ph. papatasi in the transmission of CL in Golestan Province, as well as the climate diversity of different regions in the province, the present study was carried out to examine the effect of different geographical and climatic factors (mentioned in the materials and methods section) on the distribution of Ph. papatasi.

Materials and Methods

Study area

Golestan Province is one of the 31 provinces of Iran, located in the north-east of the country, south of the Caspian Sea (53°57′-56°23′ E, 36°30′-38°08′ N) and makes approximately 1.3% of Iran's total area with a landmass of 20437.74 square km. This province is located between the three provinces of Mazandaran, Semnan and North Khorasan, is bordered by Turkmenistan from the north. The province is connected to the Caspian Sea from the east and to Alborz Mountains from the south. Weather conditions are largely diverse in various regions of the province. As such, one can experience mountainous climates in the south part of the province, arid and semi-arid climate in the north part, and mild Mediterranean climate in the western and central regions. In 2019, the province had maximum and minimum air temperatures of 40 and 20 °C, respectively, maximum and minimum relative humidity of 70 and 90%, respectively, and a rainfall amount of 333ml. It can be concluded that a wide range of suitable cli-
Sand fly collection

This analytical cross-sectional study was carried out from July to September 2014 by performing a three-time capture in a total of 34 villages (2–4 villages in each county). Sticky paper traps coated with Castor oil were used to collect sand flies. For each village, 60 indoor and 60 outdoor sticky paper traps were installed before the sunset and collected the following morning before the sunrise. All the collected sand flies were placed in acetone for two minutes and stored in 70% ethanol before transferring to the laboratory. In the laboratory, microscopic slides of the specimens were provided and the specimens were mounted in Puri’s medium. Species of all the sand flies were determined using relevant morphological keys (25-26). The data were analyzed using Spearman’s correlation test in IBM SPSS version 22.0.

Study variables

In this study, we used 22 geographical and climatic variable including: Alt; altitude from sea level (m) (Alt), Slope; slope in degrees obtained from altitude (%), BIO1: annual mean temperature (°C), BIO2: mean diurnal range (monthly mean (max temp-min temp)) (°C), BIO3: isothermality (BIO2/BIO7) (×100), BIO4: temperature seasonality (standard deviation × 100), BIO5: max temperature of warmest month (°C), BIO6: min temperature of coldest month (°C), BIO7: temperature annual range (BIO5- BIO6) (°C), BIO8: mean temperature of wettest quarter (°C), BIO9: mean temperature of driest quarter (°C), BIO10: mean temperature of warmest quarter (°C), BIO11: mean temperature of coldest quarter (°C), BIO12: annual precipitation (mm), BIO13: precipitation of wettest month (mm), BIO14: precipitation of driest month (mm), BIO15: ), BIO16: precipitation of wettest quarter (mm), BIO17: precipitation of driest quarter (mm), BIO18: precipitation of warmest quarter (mm), BIO19: precipitation of coldest quarter (mm), BIO20: normalized differentiated vegetation index.

Bioclimatic variables (n=19), environmental variables including altitude and slope, and NDVI were independent variables. The bioclimatic variables were obtained from the WorldClim global climate database (http://www.worldclim.org/current) at a spatial resolution of 1km². These variables were derived from long-term (1950–2000) monthly rainfall and temperature values for the development of significant biological variables. The environmental variables such as altitude and slope were obtained from a digital elevation model, and NDVI was obtained from MODIS satellite images in August, 2014. This study evaluated the relationship between the number of collected Ph. papatasí as the dependent variable and the independent variables. The data from the sampled villages were entered into ArcMap as a point layer, and each of the independent variables was entered into ArcMap as a raster layer. Then, each village layer was activated separately with an independent variable layer, by using spatial analyst tools and the value to point submenu, the numerical value of each independent variable in a cell, where the selected village was located, was extracted and entered into SPSS 22.0. Eventually, due to the non-normal distribution of densities of Ph. papatasí and the lack of linear regression assumptions, the relationship between the densities of Ph. papatasí with the bioclimatic variables, the environmental variables, and NDVI was examined using Spearman’s correlation test.

Results

In this study, a total of 1773 Ph. papatasí were collected from 34 villages of Golestan Province, with the highest frequency in Gonbad-e-Kavus and Maraveh Tappeh counties (Table 1). The findings show that max temperature of warmest month (°C), temperature an-
nual range (BIO5-BIO6) (°C), temperature seasonality (±SD×100), mean diurnal range (average min/max temp) (°C), precipitation seasonality (coefficient of variation), mean temperature of driest quarter (°C), and mean temperature of warmest quarter (°C) were positively associated with the density of *Ph. papatasi*. Moreover, the density of *Ph. papatasi* showed a positive inverse correlation with NDVI, but no correlation with altitude and slope (Table 2).

Table 1. Densities of *Phlebotomus papatasi* in different counties of Golestan Province, 2014

| County            | Number of selected villages | Number of collected *Ph. papatasi* | Number of collected *Ph. papatasi* for 60 traps |
|-------------------|-----------------------------|-----------------------------------|-----------------------------------------------|
| Maraveh Tapeh     | 3                           | 396                               | 132                                           |
| Gonbad-e Kavus    | 4                           | 564                               | 141                                           |
| Aqqala            | 2                           | 114                               | 57                                            |
| Ramiyan           | 2                           | 42                                | 21                                            |
| Gomishan          | 2                           | 64                                | 32                                            |
| Aliabad-e Katul   | 3                           | 156                               | 52                                            |
| Azadshahr         | 3                           | 138                               | 46                                            |
| Gorgan            | 2                           | 14                                | 7                                             |
| Kalaleh           | 3                           | 261                               | 87                                            |
| Kordkuy           | 2                           | 2                                 | 1                                             |
| Bandar-e Gaz      | 2                           | 0                                 | 0                                             |
| Bandar-e torkman  | 2                           | 10                                | 5                                             |
| Galikesh          | 2                           | 6                                 | 3                                             |
| Minudasht         | 2                           | 6                                 | 3                                             |
| Total             | 34                          | 1773                              | 52.1                                          |

Table 2. Bioclimatic and environmental variables with direct and positive correlation with densities of *Phlebotomus papatasi*.

| Correlation       | Variables                             | Mean±SD       | Correlation Coefficient | P       |
|-------------------|---------------------------------------|---------------|-------------------------|---------|
| Direct and positive | Number of collected *Ph. papatasi* 50.08±54.43 | r= 0.747     | P= 0.00            |
|                   | Max temperature of warmest month (°C) 34.06±1.16 | r= 0.529     | P= 0.002          |
|                   | Number of collected *Ph. papatasi* 50.08±54.43 | r= 0.529     | P= 0.002          |
|                   | Temperature annual range (max temp of warmest month–min temp of coldest month) (°C) 32.01±2.17 | r= 0.523     | P= 0.002          |
|                   | Number of collected *Ph. papatasi* 50.08±54.43 | r= 0.523     | P= 0.002          |
|                   | Temperature seasonality (standard deviation ×100) 7.66±0.56 | r= 0.523     | P= 0.002          |
|                   | Number of collected *Ph. papatasi* 50.08±54.43 | r= 0.466     | P= 0.006          |
|                   | Mean diurnal range (mean of monthly (max temp–min temp)) (°C) 11.52±0.87 | r= 0.465     | P= 0.006          |
|                   | Number of collected *Ph. papatasi* 50.08±54.43 | r= 0.465     | P= 0.006          |
|                   | Precipitation seasonality (coefficient of variation) 57.45±8.91 | r= 0.449     | P= 0.009          |
|                   | Number of collected *Ph. papatasi* 50.08±54.43 | r= 0.387     | P= 0.026          |
|                   | Mean temperature of driest quarter (°C) 26.81±1.08 | r= 0.387     | P= 0.026          |
|                   | Number of collected *Ph. papatasi* 50.08±54.43 | r= -0.345    | P= 0.045          |
|                   | NDVI 0.36±0.11                        |               | P= 0.007          |
|                   | Number of collected *Ph. papatasi* 50.08±54.43 | r= -0.459    | P= 0.007          |
|                   | Annual precipitation (mm) 348.42±80.26 |               | P= 0.007          |
|                   | Number of collected *Ph. papatasi* 50.08±54.43 |            | P= 0.007          |
| Table 2. Continued… |
|----------------------|
| **Direct and negative** | Precipitation of driest month (mm) | 6.78±4.41 | r= -0.497 | P= 0.003 |
| Number of collected *Ph. papatasi* | 50.08±54.43 | r= -0.552 | P= 0.001 |
| Precipitation of driest quarter (mm) | 23.93±13.56 | r= -0.497 | P= 0.003 |
| Number of collected *Ph. papatasi* | 50.08±54.43 | r= -0.590 | P= 0.00 |
| Precipitation of warmest quarter (mm) | 25.66±13.29 | r= -0.348 | P= 0.047 |
| Number of collected *Ph. papatasi* | 50.08±54.43 | r= -0.348 | P= 0.047 |
| Precipitation of coldest quarter (mm) | 120.6±22.66 | r= -0.018 | P= 0.925 |
| Number of collected *Ph. papatasi* | 50.08±54.43 | r= -0.174 | P= 0.331 |
| **Without correlation** | Altitude | 208.48±312.79 | r= 0.018 | P= 0.925 |
| Number of collected *Ph. papatasi* | 50.08±54.43 | r= 0.123 | P= 0.495 |
| Slope | 89.78±0.37 | r= -0.018 | P= 0.925 |
| Number of collected *Ph. papatasi* | 50.08±54.43 | r= -0.127 | P= 0.481 |
| Annual mean temperature (°C) | 17.20±1.15 | r= 0.123 | P= 0.495 |
| Number of collected *Ph. papatasi* | 50.08±54.43 | r= 0.123 | P= 0.495 |
| Isothermality (BIO2/BIO7) (×100) | 3.54±0.09 | r= 0.123 | P= 0.495 |
| Number of collected *Ph. papatasi* | 50.08±54.43 | r= 0.123 | P= 0.495 |
| Mean temperature of wettest quarter (°C) | 25.16±21.75 | r= -0.244 | P= 0.164 |
| Number of collected *Ph. papatasi* | 50.08±54.43 | r= -0.244 | P= 0.164 |
| Mean temperature of coldest quarter (°C) | 7.60±1.88 | r= -0.323 | P= 0.067 |
| Number of collected *Ph. papatasi* | 50.08±54.43 | r= -0.323 | P= 0.067 |
| Precipitation of wettest month (mm) | 60.06±13.27 | r= -0.285 | P= 0.108 |
| Number of collected *Ph. papatasi* | 50.08±54.43 | r= -0.285 | P= 0.108 |
| Precipitation of wettest quarter (mm) | 145.15±25.53 | r= -0.191 | P= 0.287 |
| Number of collected *Ph. papatasi* | 50.08±54.43 | r= -0.191 | P= 0.287 |
| Min temperature of coldest month (°C) | 2.05±1.93 | r= -0.340 | P= 0.053 |

*: standard deviation

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**Fig. 1.** Location of Golestan Province in Iran and collection sites for *Phlebotomus papatasi*
Discussion

The highest frequency of the collected *Ph. papatasi* was reported in Gonbad-e-Kavus and Maraveh Tappeh counties in accordance with results of a similar study conducted in Golestan Province, similarly reporting that the presence probability of this species was higher in these counties (21). These two counties are known as endemic focus for CL in Golestan Province (4-9). Moreover, the incidence of CL and the number of the rodent’s active burrows (well-known reservoir hosts of ZCL) were higher in these regions than in the other regions of Golestan Province (7, 9, 15).

Temperature was shown as one of the main factors associated with the growth and development of insects such as *Ph. papatasi* (19). The results of this study revealed that temperature significantly affected the density of *Ph. papatasi*. The densities of *Ph. papatasi* were significantly positively associated with factors such as max temperature of warmest month (°C), temperature annual range (BIO5-BIO6) (°C), temperature seasonality (standard deviation ×100), mean diurnal range (mean of max/ min temp) (°C), mean temperature of driest quarter (°C), and mean temperature of warmest quarter (°C). However, there was no significant relationship between the densities of *Ph. papatasi* with annual mean temperature (°C), isothermally (BIO2/BIO7) (×100), mean temperature of wettest quarter (°C), mean temperature of coldest quarter (°C), and min temperature of coldest month (°C). It can be concluded that max and mean temperatures of driest and warmest quarters and months were significantly associated with the density of *Ph. papatasi*. However, mean temperature of wettest and coldest quarters and months had no significant role in the density of *Ph. papatasi*, which may be due to the effect of degree-day on the growth, development, and density of different species of insects. Degree-day is a measure of the amount of heat that accumulates above a specified temperature during a 24h period (27). According to results of studies on the growth of this species, a specific temperature limit is required for growth, and temperatures higher or lower than this limit will lead to a stop of growth. The maximum temperature threshold for the growth of this species is 35 °C, and the optimal minimum temperature for the growth according to different growth stages of this species is 20, 25, and 11.6 °C. As such, oviposition activities are carried out at a temperature above 20 °C (8, 28-29). Therefore, temperature in the cold seasons, in which the air temperature does not reach 20 °C, cannot have a significant relationship with the density of this species. Colacico-Mayhugh MG et al. (23) found that max temperature of warmest month was one of the most critical factors associated with the density of *Ph. papatasi* in Eastern Mediterranean, which is supported by the findings of our study. They also showed that mean temperature of coldest quarters and min temperature of coldest month were the most influential factors in the density of this species (23); while, in our study, there was no significant relationship between the values of these variables and the densities of *Ph. papatasi*. Further, the results of the present research showed no significant relationship between the densities of *Ph. papatasi* with isothermality (BIO2/BIO7) (×100) and mean temperature of wettest quarter (°C). These variables had low effects on the density of *Ph. papatasi* in another study conducted in Golestan Province (21). However, in a study conducted in Iran (22), contrary to the results of this study, isothermality (BIO2/BIO7) (×100) and mean temperature of wettest quarter (°C) showed high impacts on the density of this species.

In addition, we found no significant relationship between annual mean temperature and densities of *Ph. papatasi*. This result is in accordance with the results of a study in Iran (22), showing a relatively low correlation between
this factor and the density of *Ph. papatasi*. While in a study conducted in Golestan Province (21), this variable showed a significant effect on the density of this species. Differences between the results of these studies and those of our study may be due to differences in the nature of these studies. All of these studies applied the MaxEnt Model as an ecological Niche model, in which modeling and prediction are based on the existence of a species in a region (30) and quantity is not measured. However, the present study analyzed the effect of each variable quantity on the densities of *Ph. papatasi* and quantity had a direct effect on the study outcomes.

Precipitation was another main factor associated with the density of *Ph. papatasi*. The findings of the current study suggested that the densities of *Ph. papatasi* were positively associated with precipitation seasonality (coefficient of variation). In other words, the increased precipitation increased the density of sand flies, which is in accordance with the results of studies conducted in Iran and other countries (22, 31-32). Rainfall influences the dynamics, reproduction, and breeding of vectors such as sandflies (33-34), as sandflies need a certain amount of moisture for their development and survival. However, heavy rainfalls can kill adults and immature stages of sand flies (35-38).

We found no significant relationship between the density of *Ph. papatasi* with precipitation of wettest quarter and precipitation of wettest month. However, Hanafi-bojd et al. (22) and Rodgers et al. (39) revealed that precipitation of wettest quarter was a major factor associated with the density of *Ph. papatasi*. Colacicco-Mayhugh MG et al. (23) revealed that precipitation of wettest quarter and precipitation of wettest month were not significantly associated with the abundance of *Ph. papatasi*, which is consistent with our study. Perhaps the reason for this is that the wettest months and quarters of the year occur in winter and sand flies have no activity in this season; with the end of the wet months of the year, the population of sand flies increases, as it was pointed out in another article (40).

Moreover, NDVI is another factor associated with the density of *Ph. papatasi*. The findings of our study revealed a significant reverse relationship between NDVI and the densities of *Ph. papatasi*, as this species is more abundant in areas with lower NDVI, which is in compliance with other studies conducted in this province and in Morocco County (15, 21, 41). Moreover, Abdel-dayme et al. (20) showed vegetation type as a major factor associated with the density of *Ph. papatasi*. Colacicco-Mayhugh MG (23) also introduced land cover as a significant factor associated with the density of *Ph. papatasi*. Moreover, Mollalo et al. (42) revealed a significant negative relationship between NDVI and the incidence of ZCL, as ZCL is more prevalent in areas with lower NDVI. Therefore, it can be concluded that NDVI is an essential factor in the incidence of ZCL.

Another factor associated with the density of *Ph. papatasi* is elevation. Accordingly, in a previous study conducted in Golestan Province, *Ph. papatasi* was collected at altitudes ranging from -32m from sea level to 598m above sea level, and densities of this species were more in plain areas with a lower altitude than in areas with a higher altitude (15). In a study conducted in Libya (20), it was observed that areas with an altitude lower than 600m were mostly suitable for the distribution of *Ph. papatasi*. Further, in a study conducted in Pakistan (43), altitude had the highest effect on the density of CL among various examined variables and *Ph. papatasi* was the dominant species in areas with a higher altitude. However, in this study, there was no significant relationship between altitude and the abundance of *Ph. papatasi*, which is inconsistent with previous studies.

Regarding slope as another factor associated with the density of *Ph. papatasi*, in different studies conducted in Golestan Province (21, 44) and Iran (22), slope was introduced
as a major factor in the density of *Ph. papatasi*. However, the findings of the present study showed no significant relationship between slope and the densities of *Ph. papatasi*.

The density of sandflies might also depend on other environmental factors, such as soil type, land-use, or wind, which can impair their flight activity (38). In the present study, we could not assess the relationship between these factors and the density of *Ph. papatasi*, which could be one of the limitations of the study.

Conclusions

Air temperature and precipitation were shown as the most important factors in the density of *Ph. papatasi* in Golestan Province as the endemic focus of zoonotic cutaneous leishmaniasis in Iran.

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