

The Seasonality of Cutaneous Leishmaniasis in Asir Region, Saudi Arabia

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Abstract

Although the incidence of Cutaneous Leishmaniasis (CL) in the Asir Region, Saudi Arabia, has decreased over the last decade, it is still a significant health problem. This study tests the hypotheses that there are relationships between climate variables (maximum, mean, and minimum temperature, rainfall, and relative humidity) and this disease in the Asir Region. Temperature was the most important factor associated with CL cases in all Asir and in the highlands of Asir during the summer and beginning of autumn. If the maximum temperature in the previous 2 to 4 months was elevated, there were more cases ($P < 0.001$). Rainfall also plays a role in CL transmission in the lowlands of Asir. There were more cases of CL if rainfall was elevated in the previous 1 to 3 months ($P < 0.05$). Based on these findings and an understanding of how CL disease is affected by climate, it should be possible to design an early warning system using the weather to predict the incidence. Therefore, the results of this study have important implications for policies to reduce this disease in the region.

Keyword: *Cutaneous Leishmaniasis, Asir Region, Saudi Arabia, climate variables*

Introduction

Leishmaniasis is an important public health problem in several countries and is considered to be the vector borne disease with the second highest number of affected people in the world after malaria (Chaves and Pascual, 2006). This disease is considered the 6th most important endemic disease in the world by the World Health Organisation (World Health Organization, 2007). One of the most common forms, cutaneous leishmaniasis, is rarely fatal but it can lead to tissue destruction, scarring, and serious visible impairment. These can lead to social stigma due to deformation of the face with permanent scarring (CFSPH, 2009; Murray et al., 2005; Reithinger et al., 2007;).

Leishmaniasis is a group of zoonotic diseases transmitted to humans and animals by the bite of phlebotomine sandflies. The infective agents are several species of flagellated protozoan parasites (Reithinger et al., 2001). There are more than 1,000 known species of sandfly in the world, of which only 70 species are known to transmit diseases such as Leishmaniasis (Murray et al., 2005). Only female phlebotomine sandflies suck blood, leading to Leishmaniasis. Sandflies do not make noise when they fly and are also small, being around one-third the size of a mosquito. Their bite is also painless (CDC, 2010). This means that people may be unaware of sandflies and their biting. Cutaneous Leishmaniasis causes skin sores caused by leishmania major. It is common in rural areas, with

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dogs and bush mammals being reservoir hosts. Another cause of CL tropica is more common in urban areas and leads to CL in humans and dogs (Wittner et al., 2000).

Leishmaniasis is distributed in around 90 countries of the world, most of which are in the developing countries (16 developed countries and 74 developing countries), and there are approximately 350 million people at risk of leishmaniasis in these areas (Cardenas et al., 2006; Schrieffer et al., 2009). Tropical and subtropical countries are the most affected by this illness (World Health Organization, 2007). More than 90% of CL occurs in parts of Afghanistan, Algeria, Iran, Iraq, Saudi Arabia, Syria, Brazil, and Peru (CDC, 2010; TDR, 2002).

There are only a few studies that look at the direct influence of weather upon leishmaniasis cases. However, there is good evidence of a close linkage between the abundance of sandflies and leishmaniasis cases (Al-Amru, 2002; Al-Tawfiq and Abu-Khams, 2004; Abdulwahab and Abdulmehsen 2005).

The literature review relating climate variables to CL highlights a number of important points. A wide range of study designs have been used to investigate the relationships between leishmaniasis and weather. These range from purely observational (e.g. more leishmaniasis in summer), but very few conduct statistical analyses of leishmaniasis cases and associations with weather. Numerous different climate variables have been used in previous studies, including temperature, rainfall, wind, and relative humidity. Most, but not all studies, showed that climate variables have an impact upon CL incidence (Cross and Hyams, 1996; Faulde et al., 2008; Franke et al., 2002). However, the impact of specific climate variables can be either positive or negative depending upon the geographical setting and season. Lagging the weather variables is an important feature of these studies.

Many studies support these findings by showing that weather influences the abundance of the leishmaniasis vector (sandfly). Others found that the vector abundance has an effect upon the incidence of leishmaniasis.

Weather conditions are not the only factors that can affect Leishmaniasis. There are many other

factors, such as ecological and environmental conditions, social, and economical determinants (El-Badry et al., 2009; Faulde et al., 2008).

There have been few studies in Saudi Arabia focusing upon the influence of weather on this disease (Al-Tawfiq and Abu-Khams, 2004; El-Badry et al., 2009; Abdulwahab and Abdulmehsen 2005; Ministry of Health KSA, 2008). These studies suggest a 2-6 month lag between weather and cases. This lag also depends on the type of leishmaniasis. Based on the findings of this study and an understanding of how CL is affected by weather, it should be possible to design an early warning system to predict incidence in Asir Region. This would be useful for health service planning for example, identifying periods when enhanced insecticide spraying is required. Also, if weather alters under climate change then this data could help predict the impact of this change on CL in Asir Region. It improves our understanding of disease transmission dynamics in this region.

Material and Methods

Data: The numbers of CL cases in each month, from the first of January 1996 to the end of December 2007 for the whole of the Asir Region, Saudi Arabia, and each endemic sector, were obtained from the Vector Control Administration, Health Affairs Directorate in Asir. Weather data (maximum, mean, and minimum temperature, rainfall, and humidity) were collected from Khamise city. This city is the second main city in the region and covers the largest occupied sector in the middle of the region.²² These data were obtained from The Centre of Information and Documentation in the Meteorological and Environmental Protection section of the Ministry of Defence and Aviation in Saudi Arabia. Other weather data for the lowlands were obtained from Majaredah (maximum and minimum temperature for 132 out of 144 months) and Rejal-Alma (rainfall for 132 out of 144 months) from the Ministry of Water and Electricity (MEPS, 2007).

Topographically, climatically, and endemically, this region can be divided into three main sectors for CL (Gaafar et al., 1998; MEPS, 2007). (Figure 1).

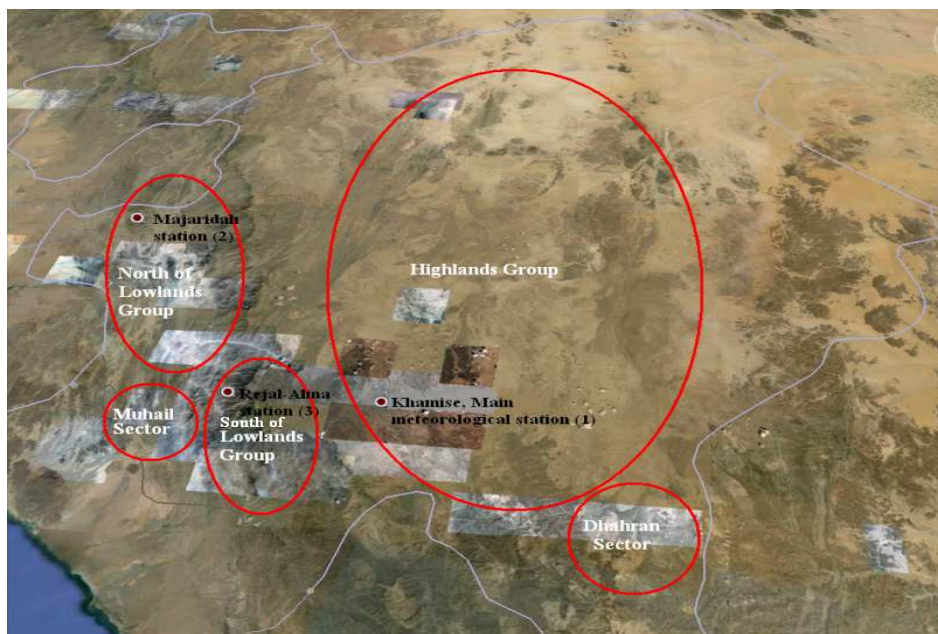


Figure 1: Topographic Map of Asir Region

1. Asir Sarawat Mountains (a part of Highlands Group): A series of high mountains extending from the north of Asir Region to the south along the coastal plains of the Red Sea (2000 - ~3000m above sea level). This area covers districts such as Abha, Khamise, Tanoma, and Dhahran. The annual average temperature for this sector is 17.7°C, average rainfall is 512mm (the highest rainfall in Saudi Arabia), and annual average relative humidity is 53.1%. These areas have the highest occurrence of leishmaniasis in the Asir Region and *P. arabicus* specie is the main vector.
2. Asir Plateau (a part of Highlands Group): In the NE Asir with an elevation range between 1,000 and 2,000m decreasing to the east, this area covers districts such as Tathlith, Bishah, and Tareeb. The annual average temperature for this sector is 19.50C with 250mm annual rainfall and an annual average relative humidity of 44.4%. This sector has many wadies that all flow eastward. It has little leishmaniasis incidence and *P. arabicus* specie is the main vector.
3. Tehama (Lowlands Group): Receives an annual rainfall of more than 500mm and temperature ranges between 250C and 490C, and the

relative humidity varies from 55% in summer to 70% in winter. This area can be divided into two sections:

- a. Foothills such as Al-Majaredah, Muhail, and Rejal-Alma, where the altitude is between 300 and 900m. This area has the highest occurrence of leishmaniasis after the highlands in Asir Region and *P. papatasi* specie is the main vector.
- b. Red Sea Costal Plain (RSCP), such as Al-Gahma, Al-Berk, and Al-Huraidah. The altitude in this area is between 0 and 200m. The lowest leishmaniasis occurs in the region, and *P. papatasi* specie is the main vector.

There are wide differences in topology and weather within Asir. Consequently, there are likely to be differences in leishmaniasis incidence and seasonality between sectors. To investigate this further, the overall incidence rates and histograms of CL were produced for each of the sectors within Asir. Data exists for nine sectors: Abha, Khamise, Sarat-Abedah, Muhail, Majaredah, Rejal-Alma, Dhahran-Aljanoub, Tanoma, and Sabet-Alalia. One sector was not included in the analysis (Ahad-Rifadah), as it only had a few cases during the

period of this study (8 cases). For the analysis, four models were constructed. The first was an analysis of CL in all Asir against Khamise weather data (Station 1 Figure 1). The following sectors were grouped together based upon sectors with similar seasonal patterns. The first group is the Highlands Group, which includes CL cases in 7 sectors: Abha, Khamise, Sarat-Abedah, Tanoma, and Sabet-Alalia against Khamise weather data (Station 1 Figure 1). The second group is the Lowlands Group, which includes CL cases in Majaredah and Rejal-Alma against Majaredah temperature and Rejal-Alma rainfall (Station 2&3 Figure 1). The third Group is from different lands, including Muhail and Dhahran-Aljanoub. The data for the third group has not been analysed due to the low number of cases reported during the study period. Also, no representative weather data exists for this group of sectors.

Data Description: The monthly averages of CL cases in the whole of Asir Region, the highlands group, the lowlands group, during the study period are presented in Figure 2. There is a clear seasonality with peak incidence between October and March for the whole Asir (Figure 2-A) and the highlands (B) with peak averages of cases between October and March. However, there is much less seasonality in the lowlands (C) with the peak cases occurring between February and June.

The weather data for Khamise will be used in the analysis of cases across the whole of Asir Region as well as the highlands group. The temperature in Majaredah and rainfall in Rejal-Alma will be used as representative of conditions in the lowlands group (See Figure 1). The highest average maximum temperature in the highlands (Figure 3A) and lowlands (Figure 3B) occurs in June (32.3 and 41.98°C respectively). The lowest average minimum temperature in the highlands and lowlands occurs in January (8.5 and 20.34°C respectively).

The monthly average rainfall in the highlands (Khamise) shows peak rainfall between March and August with the highest occurring in April and minimum occurring in February (Figure 4A). The monthly average rainfall in the lowlands (Rejal-Alma) shows seasonality with peak rainfall between December and April (Figure 4B). The highest averages were in March. The average rainfall during the summer and autumn are lower

with the lowest averages occurring in October. The monthly average relative humidity in the highlands (Khamise) shows a peak during the months of November to March with the highest percentage occurring in January and the lowest percentage of humidity in September (Figure 5).

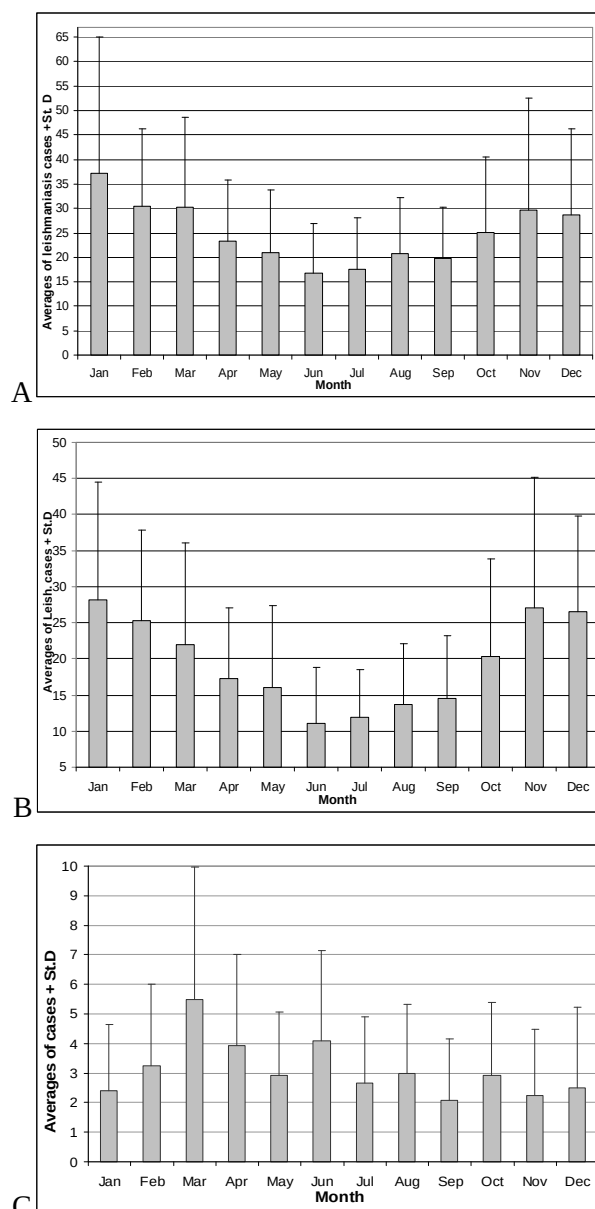


Figure 2: Monthly Averages of CL Cases in the Whole of Asir (A), the Highlands (B) and the Lowlands (C)

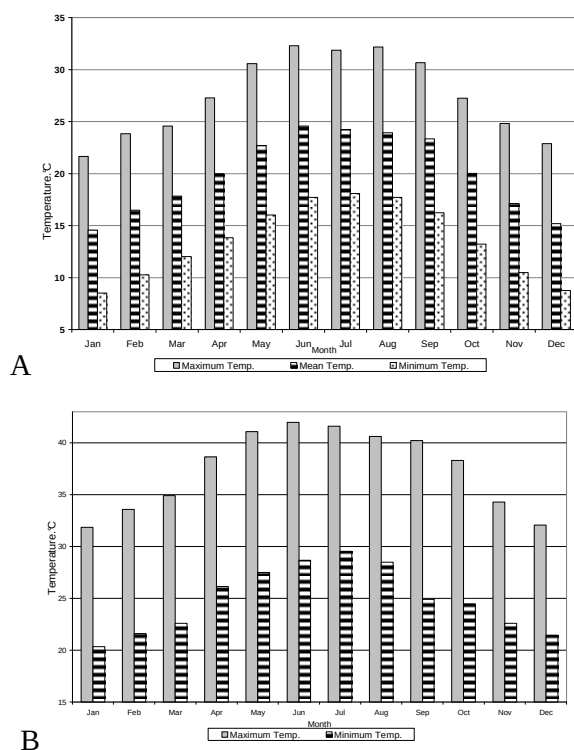


Figure 3: Maximum, Mean, and Minimum Average Temperatures in the Whole of Asir and the Highlands (A) and Maximum and Minimum Average Temperature in the Lowlands (B) (1996 - 2007)

Data Preparation: The analysis to examine the relationship between monthly cases of CL and the selected weather data proceeded in a number of stages. Due to a positively skewed distribution of the number CL cases, the natural logarithm (Ln) of CL cases (adding 1 to zero values) was performed for the cases to produce Ln CL. For similar reasons, the natural logarithm was taken of rainfall (adding 1 to zero values) to produce Ln rainfall.

In order to control for this effect, for the whole of Asir, the highlands and lowlands data and the natural logarithm of CL cases was put into a regression against time (each month numbered from 1 to 144). The unstandardised residual from this model represents the natural logarithm of CL cases with the long term trend in incidence removed.

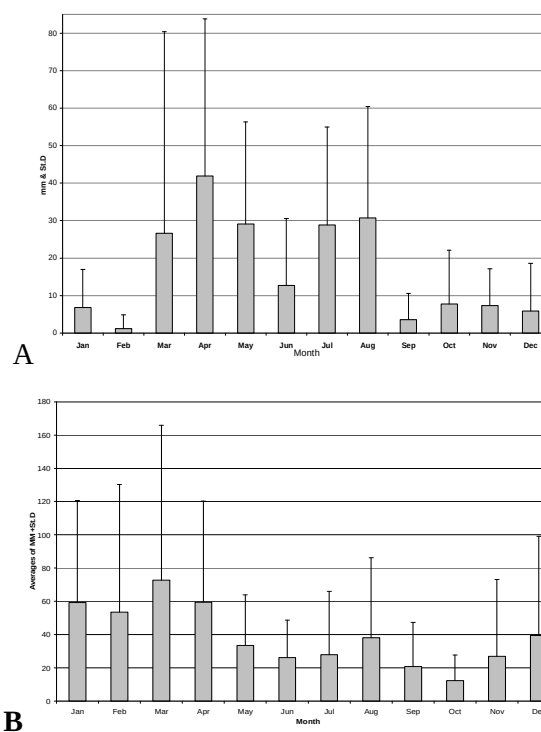


Figure 4: Monthly Average Rainfall in the Whole of Asir and the Highlands (A) and in the Lowlands (B) (1996 - 2007)

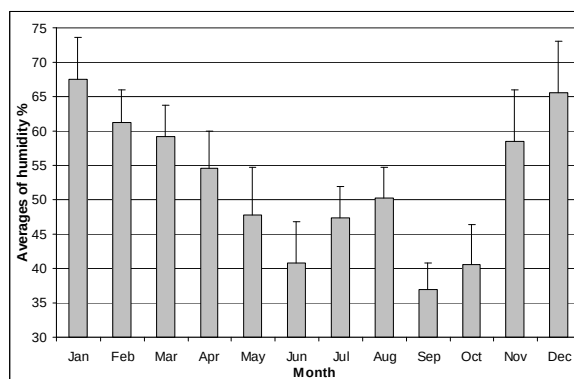


Figure 5: Monthly Average Relative Humidity in the Whole of Asir and the Highlands

Statistical Analysis: The literature review has demonstrated that the relationship between CL cases and weather may vary according to the time of the year. Therefore, the analysis proceeded in stages:

- In the first stage, scatter plots were created of the detrended (DT) natural logarithm of Cuta-

neous Leishmaniasis (DT Ln CL) against each of the weather variables.

- b. Within each group (all Asir, highland, lowlands), months were grouped together. The models for all Asir and the highlands region consider three time periods: February to May, June to September, and October to January. The results for the lowlands region are presented for two time periods: March to November and December to February. The grouping for all Asir, highlands and lowlands, for each period was dependant on the pattern of cases throughout the year.
- c. To produce an analysis that is more robust to the distribution of the data, an ordinal logistic (OL) of Ln CL cases for every month against each of the weather variables was produced as well. This was achieved by dividing Ln CL into five categories with equal numbers of months.
- d. In the regular regression analysis it was not possible to assume that the CL rate in one month is unrelated to the CL rate in the next month (i.e. the data is autocorrelated). Therefore, all models were analyzed in three ways. The first did not control for seasonality or autocorrelation. The second controlled for seasonality by incorporating dummy variables for each of the individual months. The final controlled for autocorrelation by adding the CL cases in the previous months into these models.
- e. The same actions were repeated for the ordinal logistic analysis.
- f. The regressions were performed against the current month's weather data as well as the previous month's weather data up to 6 previous months. The literature review indicated that lagged relationships may exist up to this period. We then examined these relationships and combined the weather from the three months with the strongest associations with CL.
- g. In most cases, the strongest relationships were between DT Ln CL and temperature in 2-4 previous months and between DT Ln CL and rainfall in 1-3 previous months. Therefore, for consistency these lags were used in all models.

All of the data were analyzed using SPSS v.16/ v.18 for Windows and Microsoft Excel 2007 / 2010.

Results

The analysis is presented by first looking at relationships between CL and temperature (maximum, mean, and minimum) followed by rainfall and relative humidity. This is performed for all of the Asir region, the highlands, and the lowlands separately.

In the result we have used 0P to represent the models where the independent variables are not lagged, 1P represents the independent variables lagged by 1 month, and so on until 6P. Linear regressions and ordinal logistic of DT Ln CL cases against each weather data were performed. The result will be presented from the normal and multiple regressions for the coefficient of DT Ln CL cases against averages of three main variables of weather data.

For temperature, we will present maximum temperature only as it has a similar seasonality to minimum and mean temperature and appeared to have the strongest associations with CL. In the multiple regressions we will present only models for times of the year when one of the independent variables was significant.

A- Regression of CL in All Asir: The strongest results from the univariable linear and ordinal logistic regression for CL in all Asir against maximum temperature, rainfall, and relative humidity, for average of 2, 3, and 4 previous months during June to September period are illustrated in Table 1. Table 2 presents the multiple regressions for all combinations of these variables.

The results of multiple regressions for CL in Asir during June to September demonstrated that in no models were more than one weather variable significant. We conclude therefore that the best model for period is that of DT Ln CL against maximum temperature in the previous 2-4 months. This temperature variable was positively significant in all variants of the normal and ordinal logistic regression. In all cases, models including this variable had a better fit (adjusted R^2 and log likelihood ratio) and a stronger significance than any of the other weather variables. Higher maximum temperature was associated with elevated CL cases.

Table 1

Normal Regressions of DT Ln CL Cases of Asir for Maximum Temperature, Rainfall and Relative Humidity during June to September for Average of 2 to 4 Previous Months

Average of 2-4 previous months	Linear Regression: Variables Only			With Seasonality		With Auto Correlation & Seasonality		Ordinal Logistic: Variables Only			With Seasonality		With Auto Correlation & Seasonality	
	Cof.	P		Cof.	P	Cof.	P	Cof.	P		Cof.	P	Cof.	P
Max.Tem. Only	.055	.003		.221	.001	.247	.001	.323	.030		.432	.032	.851	.034
Rainfall Only	-.130	.043		-.158	.056	-.162	.055	-.512	.166		-.777	.068	-.845	.061
Humidity Only	-.024	.031		-.030	.080	-.030	.089	-.056	.169		-.069	.271	-.168	.168

Cof. : Coefficients. P: P value (= or <).

Table 2

Multiple Regressions of DT Ln CL Cases of Asir for Maximum Temperature, Rainfall, and Relative Humidity during June to September for Average of 2 to 4 Previous Months

Average of 2-4 previous months	Linear Regression: Variables Only			With Seasonality		With Auto Correlation & Seasonality		Ordinal Logistic: Variables Only			With Seasonality		With Auto Correlation & Seasonality	
	Cof.	P		Cof.	P	Cof.	P	Cof.	P		Cof.	P	Cof.	P
Max.Tem.	.059	.001		.183	.005	.207	.002	.153	.049		.169	.044	.600	.024
Rainfall	-.151	.010		-.088	.214	-.091	.192	-.605	.107		-.638	.248	-.554	.283
Max.Tem.	.008	.016		.183	.009	.217	.003	.019	.050		.303	.048	.411	.041
Humidity	-.021	.113		-.012	.344	-.009	.477	-.053	.478		-.040	.602	-.127	.167
Rainfall	-.022	.002		-.114	.173	-.124	.144	-.457	.217		-.792	.138	-.357	.532
Humidity	-.103	.078		-.020	.138	-.020	.156	-.049	.224		.004	.963	-.133	.158
Max.Tem.	.083	.045		.170	.018	.204	.006	.178	.027		.201	.039	.361	.031
Rainfall	-.136	.038		-.072	.365	.086	.277	-.633	.144		-.752	.640	-.291	.618
Humidity	-.007	.607		-.006	.667	-.002	.901	.011	.898		.020	.819	-.103	.323

B- Multiple Regression of CL in Highlands

Group: The strongest results from the univariable linear and ordinal logistic regression for CL in the highlands against maximum temperature, rainfall, and relative humidity for the average of the previous 2-4 months during June to September are illustrated in Table 3. Table 4 presents the multiple regressions for all combinations of these variables.

The results of the multiple regressions for CL in the highlands during June to September demonstrated that no models with more than one weather

variable were positively significant. We conclude therefore that the best model for this period is that of DT Ln CL against maximum temperature in the previous 2-4 months. This weather variable was positively significant in all variants of the normal linear and ordinal logistic regressions and in all cases had a better fit (adjusted R^2 and log likelihood ratio) and a stronger significance than any of the other weather variables. Higher maximum temperature was associated with elevated CL cases.

Table 3

Normal Regressions of DT Ln CL Cases of the Highlands for Maximum Temperature, Rainfall and Relative Humidity during June to September for Average of 2 to 4 Previous Months

Average of 2-4 previous months	Linear Regression: Variables Only				With Seasonality				With Auto Correlation & Seasonality			
	Cof.	P	Cof.	P	Cof.	P	Cof.	P	Cof.	P	Cof.	P
Max.Tem. Only	.073	.005	.262	.002	.278	.001	.164	.047	.512	.033	.718	.036
Rainfall Only	-.096	.289	-.175	.080	-.178	.079	-.110	.765	-.411	.339	-.345	.427
Humidity Only	-.022	.026	-.018	.288	-.017	.309	-.048	.266	-.029	.663	-.084	.249

Table 4

Multiple Regressions of DT Ln CL Cases of the Highlands for Maximum Temperature, Rainfall and Relative Humidity during June to September for Average of 2 to 4 Previous Months

Average of 2-4 previous months	Linear Regression: Variables Only				With Seasonality				With Auto Correlation & Seasonality			
	Cof.	P	Cof.	P	Cof.	P	Cof.	P	Cof.	P	Cof.	P
Max.Tem.	.077	.003	.245	.012	.263	.008	.177	.024	.440	.039	.740	.042
Rainfall	-.123	.143	-.040	.706	-.034	.747	-.222	.554	.176	.714	.046	.927
Max.Tem.	.085	.036	.314	.003	.355	.001	.206	.030	.632	.035	.676	.040
Humidity	.006	.764	.016	.381	.023	.235	.019	.814	.037	.652	-.012	.891
Rainfall	-.069	.430	-.175	.168	-.183	.156	-.083	.823	-.461	.385	.676	.040
Humidity	-.021	.037	.001	.994	.001	.944	-.047	.174	.014	.871	-.012	.891
Max.Tem.	.129	.019	.295	.006	.336	.003	.297	.020	.579	.019	.697	.040
Rainfall	-.170	.073	-.104	.384	-.116	.237	-.330	.433	-.344	.524	.091	.869
Humidity	.023	.271	.025	.242	.032	.135	.052	.572	.064	.409	.019	.847

C- Multiple Regression of CL in Lowlands

Group: The strongest results from the univariable linear and ordinal logistic regression for CL in the lowlands against maximum temperature and rainfall in the previous 1-3 months are illustrated in Table 5. Table 6 presents the multiple regressions for all combinations of these variables.

The results of multiple regressions for CL in the lowlands group during March to November demonstrated that in no models was more than one weather variable significant. We conclude therefore that the best model for this period is that of DT Ln CL against rainfall. Average rainfall in the previous 1-3 months between March and November was positively significant in all variants of the

normal linear and ordinal logistic regression and in all cases had a better fit (adjusted R^2 and log likelihood ratio) and a stronger significance than maximum temperature. Higher rainfall was associated with elevated CL.

Discussion and Conclusion

There are two main species of leishmaniasis cases in Saudi Arabia: VL and CL (Al-Amru, 2002). This study focuses on CL in Asir Region, as this form of illness is endemic and spread over the foothills and highlands of this region.

Table 5

Normal Regressions of DT Ln CL Cases of the Lowlands for Maximum Temperature and Rainfall during March to November for Average of 1 to 3 Previous Months

Average of 2-4 previous months	Linear Regression: Variables Only			With Seasonality			With Auto Correlation & Seasonality			Ordinal Logistic: Variables Only			With Seasonality			With Auto Correlation & Seasonality		
	Cof.	P		Cof.	P		Cof.	P		Cof.	P		Cof.	P		Cof.	P	
Max.Tem. Only	-.038	.010		.048	.426		.032	.587		-.137	.019		-.045	.843		-.018	.939	
Rainfall Only	.099	.004		.085	.012		.078	.022		.800	.001		.829	.001		.492	.008	

Table 6

Multiple Regressions of DT Ln CL Cases of the Lowlands for Maximum Temperature and Rainfall during March to November for Average of 1 to 3 Previous Months

Average of 2-4 previous months	Linear Regression: Variables Only			With Seasonality			With Auto Correlation & Seasonality			Ordinal Logistic: Variables Only			With Seasonality			With Auto Correlation & Seasonality		
	Cof.	P		Cof.	P		Cof.	P		Cof.	P		Cof.	P		Cof.	P	
Max.Tem.	-.028	.070		.035	.567		.023	.710		-.067	.322		.213	.443		.120	.665	
Rainfall	.097	.006		.086	.012		.080	.022		.853	.001		.893	.001		.565	.005	

The literature review in this region state that the distribution of this disease in Asir region is influenced by some little known climate factors and geographical situation (Al-Zahrani et al., 1989; Abdulwahab and Abdulmehsen 2005).

There were some difficulties during this study, as we only had limited data for weather in the selected areas in Asir. For example, the weather in Khamise is not representative of the whole of Asir, as the elevation in this region varies from 0 to 3000m. Weather, and hence sandfly distributions and leishmaniasis cases, are almost certain to vary across Asir. Also, it was not possible to analyse the data for some sectors due to lack of weather data and the low number of cases. For example, no weather data was available for the Different Lands Group, and the numbers of cases reported for this sector was low. Finally, some of the leishmaniasis cases were unclassified and so could not be assigned to a sector.

Overall, the CL cases show that the total number of yearly cases is declining from a peak (outbreak) in 1998. This outbreak may have been due to the

heavy rainfall throughout this region during some months of years 1997 and 1998 (Al-Amru, 2002). However, our results indicated that rainfall is not associated with CL cases in the highlands area where most cases occur. Vector control is a likely explanation for this reduction in cases.

The statistical analysis was based on the hypothesis that there is a relationship between weather and CL. This was assumed because the distribution of leishmaniasis is tightly linked to geography and may be sensitive to weather and climate influences (Reithinger et al., 2007). There is also evidence that climate affects sandfly numbers, which has an impact upon leishmaniasis cases. The vector is affected by environmental conditions, especially temperature and rainfall (Cross and Hyams, 1996). A study in Argentina showed that the activity season of one sandfly species sharply increased during the rainy season and decreased during the months of lower rainfall or higher temperatures (Reithinger et al., 2007). The increased rainfall can lead to an increase in vegetation, allowing expansion in the population of vertebrate host (Hunter 2003). An increase in

sandfly populations can lead to an increase in the occurrence of leishmaniasis (Gage et al., 2008). There is therefore much evidence that weather is important for leishmaniasis.

Monthly averages of CL cases in all Asir Region during the study period show transmission throughout the year. However, there is a clear seasonality with peak incidence between October and March, with the highest average number of cases in January. The average number of cases during the summer is lower, with the lowest number of cases in June. There was a high standard deviation in most months which indicates that there is a large variability from year to year in monthly CL cases. Most of the CL cases in Asir are in the first group (highlands) so the monthly patterns of cases are similar between the two. There is much less seasonality in the lowlands than in the highlands group with the peak cases occurring between February and June with the highest cases in March. Case numbers in the rest of the year are little lower, with the lowest cases in September.

In the results, CL incidence was compared to temperature across Asir. The results presented evidence that temperature is an important factor affecting variation in CL cases, but only during the summer (June to September). Elevated maximum temperature in the 2-4 previous months was highly significantly associated with leishmaniasis cases ($P < 0.001$). This result was nearly identical in the highlands group, which is unsurprising as most cases in Asir occur in the highlands. This result is plausible as the lags indicate that temperature during the end of winter and early spring affects leishmaniasis cases in the summer. During the end of winter and early spring, temperatures are generally low (around 10 to 20°C) so elevated temperatures may have positive effects upon the vector. There was no effect in the lowlands indicating that temperatures are never a limiting factor for leishmaniasis. In the lowlands, winter temperatures are usually higher (20 to 25°C). The influence of temperature is supported in the literature and Cross et al. (1996) state that the vector is affected by environmental conditions, especially temperature. There are some possible mechanism changes in the influence of temperature on the transmission of vector borne disease (Gubler et al., 2001; Hunter, 2003). Most of the CL

cases in this study are from highland areas, and the highest average maximum temperature in the representative area occurs in June. In some parts of India one of the studies revealed that the sandfly were found only at temperatures between 17 and 36°C (Singh, 1999). Therefore, the highlands might provide the optimum temperature for the vector during summer, and then the activity of sandfly is likely to increase with this temperature.

The study shows that the increase of temperature during summer can lead to an increase of CL cases in the whole of the Asir Region and also in the highlands group. However, there was no evidence for a relationship between maximum temperature and CL cases in the lowlands group. This is slightly unexpected, as the highest average maximum temperature occurs in June which reaches over 40°C. Adults and larvae are sensitive to high temperature, and in laboratory experiments, all adult sandflies died within two hours at temperatures above 40°C (Cross et al., 1996). A negative association with maximum temperature in the summer might therefore be expected. The lack of a result suggests that sandflies find mechanisms to avoid these high temperatures

Maximum, mean, and minimum temperatures in Asir are highly correlated. However, maximum temperature in Asir was most strongly associated with leishmaniasis cases. This suggests that maximum temperature is most related to the temperatures experienced by the sandflies, but the reasons for this are unclear.

Within the whole of Asir and in the highlands, there was no evidence that rainfall impacted on CL cases. This may indicate that rainfall has no impact or influence on the species of sandflies in the highlands. In the lowlands group, there was evidence that increased rainfall can lead to increased cases of leishmaniasis. There is a highly positive significant relationship between the average rainfall in the 1-3 previous months and CL cases (between March and November). This indicates that rainfall provides suitable conditions for the vector, but in the lowlands only. Hunter (2003) noted that increased rainfall can increase vegetation growth and allow expansion in the population of vertebrate hosts; therefore, this can increase the infected sandfly numbers and thus the possibility of CL cases. MOH in Saudi Arabia, 2000 has mentioned that there is a highly

significant correlation between the density of sandfly and positive cases. This is because after rainfall, it takes time for increases in sandflies to occur.

In Pondicherry, India, summer rainfall is followed by an increase in the population of sandflies (Srinivasan et al., 1993). Also, some studies in Colombia stated that drought followed by rainfall increases the occurrence of CL (Cardenas et al., 2006; Gage et al., 2008). The vector is affected by rainfall (Cross and Hyams, 1996). Therefore, these conditions can lead to increase the vector, thus the occurrence of CL. Our results suggest that in the lowlands area of Asir there is not enough rainfall for vegetation. This means that when there is rainfall there are more sandflies and hence leishmaniasis. The weather in these areas is drier. It is therefore not surprising that more rainfall may lead to more vegetation and hence more sandflies and leishmaniasis.

Some studies note that humidity is one of the most important weather factors for sandfly survival, development, and activity (Cross et al., 1996; Kasap et al., 2009; Srinivasan et al., 1993), but the results of this study do not show evidence that there was a significant relationship between relative humidity and CL cases for Asir or any of the endemic areas. This interpretation is slightly limited by the absence of humidity data in the lowlands. This contradiction could be due to the different location of this study. It also could be due to the increase in humidity, which is associated with other weather factors, such as high temperature, which have shown themselves to be significant in the model.

In summary, this study showed that weather factors play an important role in affecting CL cases.

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Temperature was the most important factor associated with CL in all Asir and in the highlands area during the summer and beginning of autumn. If the maximum temperature in the previous 2 to 4 months was elevated, there were more cases. Rainfall plays an important role in CL transmission in the lowlands with greater cases if rainfall is elevated in the previous 1 to 3 months. This occurs in all months except during the winter season. Although this study shows that weather has an influence upon CL in Asir, it is important to recognize that leishmaniasis cases are becoming less of a problem in this region. Overall, the study shows that the total number of yearly CL cases has declined to one third of cases in the nineties by the end of the study period.

Based on these findings and an understanding of how CL disease is affected by climate, it should be possible to design an early warning system using the weather to predict the incidence of this disease. Therefore, the results of this study have important implications for policies to improve public health in this region.

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