Brooker, S; Mohammed, N; Adil, K; Agha, S; Reithinger, R; Rowland, M; Ali, I; Kolaczinski, J (2004) Leishmaniasis in refugee and local Pakistani populations. Emerging infectious diseases, 10 (9). pp. 1681-4. ISSN 1080-6040 DOI: https://doi.org/10.3201/eid1009.040179

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DOI: 10.3201/eid1009.040179

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Leishmaniasis in Refugee and Local Pakistani Populations

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The epidemiology of anthropogenic cutaneous leishmaniasis was investigated in northwest Pakistan. Results suggested similar patterns of endemicity in both Afghan refugee and Pakistani populations and highlighted risk factors and household clustering of disease.

In Central Asia, anthropogenic cutaneous leishmaniasis (ACL) is commonly caused by Leishmania tropica and characterized by large, chronic, and disfiguring skin ulcers, which often cause severe social stigma. Because ACL is transmitted anthropogenically (i.e., from human to human) by sandflies, the infection can spread rapidly in concentrated populations, particularly under poor housing conditions, i.e., overcrowding or lack of protection from bloodsucking insects. In Afghanistan, the incidence of endemic but sporadic ACL has dramatically increased during decades of civil war, because of the associated deterioration of the infrastructure and migration (1–3). Less is known about the current distribution of the disease in neighboring Pakistan, where it has always been widespread but considered “patchy” and nonendemic (4). Recently, however, local authorities and nongovernmental health providers have reported an increasing number of ACL cases in Afghan refugee camps (5,6), which causes concern about the potential spread of the disease among the population and local Pakistani villagers. Therefore, a large-scale epidemiologic study was conducted throughout northwest Pakistan to investigate this issue.

The Study

From December 2002 to March 2003, a study was conducted in 48 Afghan refugee camps and 19 neighboring villages in Balochistan and North-West Frontier Province (NWFP), Pakistan. Refugee camps were selected on the basis of past and present ACL cases reported by healthcare providers. Villages within 1 km of selected camps were included in the survey; if multiple villages were within 1 km of a camp, one with reported ACL cases was randomly selected, although this method may have introduced selection bias. The goal of the study was to estimate the prevalence of ACL in Afghan refugee camps and neighboring Pakistani villages, as well as determine whether refugee camps could be the source of the anecdotal rise in ACL cases in neighboring villages. In each site, 40 households were sampled along east-west and north-south perpendicular transects. Every head of household was interviewed with a standard questionnaire. If a family reported cases of ACL, an interviewer who had been trained in clinical ACL diagnosis asked to inspect the lesions. Because of logistic constraints, no parasitologic confirmation was performed, but lesions caused by organisms other than Leishmania are rare, and our previous studies have shown that specificity of our clinical diagnosis is 73%–76% (5).

The study included 21,046 persons in 48 refugee camps and 7,305 persons in 19 neighboring villages. Overall, 650 persons (2.3%) had ACL lesions only, 1,236 (4.4%) had ACL scars only, and 38 persons had both ACL lesions and scars. Of those with active ACL, the mean lesion number was 2.1 (range 1–16), and the mean lesion duration (to survey date) was 5.1 months (range 0.7–50 months). Using maximum likelihood methods (7), we estimated the average annual force of infection of ACL to be 0.01 per year (10 cases/1,000 persons per year) during the past 6 years.

In refugee camps, the prevalence of ACL lesions was 2.7%, and prevalence of scars was 4.2%. In neighboring Pakistani villages, the prevalence of ACL lesions was 1.7%, and prevalence of scars was 4.9%. Lesion prevalence increased with age more markedly among local Pakistanis than Afghan refugees until children were 5–6 years of age; then the prevalence of lesions decreased among Pakistanis and was lower than in the Afghan refugee population for all remaining age groups (Figure). These age trends suggest past infection and resultant immunity. Had the disease been introduced more recently, the risk of ACL would not be expected to be related to age, since everyone would be susceptible to infection (8). However, the low prevalence of scars relative to the number of active lesions, especially among adults, suggests that the disease has been endemic in the region for a short period of time and that transmission may be characterized by a prolonged epidemic similar to that found in Kabul (2,4).

To examine the association with potential risk factors and to take clustering of persons within households into account, univariate odds ratios (OR) were estimated by logistic regression with robust standard errors. We used backward stepwise multiple logistic regression to identify significant explanatory risk factors while controlling for other variables. Spatial clustering of ACL was investigated...
at the household and village levels. The degree of within-
household clustering was calculated by using a random-
effects model fitted to a logistic regression to account for
the nonindependence of persons within households. The
analysis was conducted using STATA 8 (Stata Corporation,
College Station, TX). The nonparametric Mantel correla-
tion statistic with Mantel 2 (Queensland University of
Technology, Brisbane, Australia) was used to assess spatial
correlation in prevalence between settlements by investi-
gating the relationship between differences in lesion preva-
lence and geographic distances.

The univariate analysis showed that an increased risk of
ACL lesion was associated with years lived in camp or vil-
lage, a family member visiting Afghanistan in the last 12
months, household members with ACL lesions, household
members having ACL scars, age group, household with
stone walls, crowding in the household (i.e., the number of
people per room), having cows in a compound, and having
dogs in a compound (Table 1). The same variables were

Figure. A) Proportion of unscarred population with active lesions
by age and settlement type. B) Proportion of population with scar
by age and settlement type.

significantly associated with the risk of having an ACL
scar, with the exception of a family member’s having vis-
ited Afghanistan in last 12 months. Use of a mosquito net
was associated with an increased risk of having a scar. Mul-
tivariate analysis showed that younger age, as well as
ACL lesions in other household members, increased the
risk of an ACL lesion (Table 2). Increased risk of an ACL
scar was associated with younger age, living in a refugee
camp, and scars in other household members. No signifi-
cant interactions were detected among the other variables
included in the analysis. Finally, after age, sex, and house-
hold factors were adjusted for, the random effects model
found evidence for significant household clustering of
active ACL cases: \( \rho = 0.54 \) (95% confidence interval [CI]
0.49–0.59, \( p < 0.0001 \)). ACL scars clustered in households
to an even greater degree: \( \rho = 0.62 \) (95% CI 0.59–0.65, \( p < 0.05 \)). The prevalence of ACL lesions showed a marked
variation (0%–21.9%) between Afghan refugee camps and
neighboring Pakistani villages. However, analysis using
the Mantel correlogram indicated no spatial structuring of
ACL between neighboring villages, which emphasizes the
highly focal distribution of ACL transmission at the village
level and corroborating significant household clustering of
ACL.

Conclusion

The analysis of putative risk factors for ACL indicated
that living in a stone house reduced the risk, whereas the
presence of cows and dogs increased it (Table 2). Although
dogs have been found infected with \( L. \) tropica (9), they are
probably not leishmaniasis reservoirs, as transmission of
\( L. \) tropica is thought to be anthroponotic (2). Instead, dogs
and other domestic animals represent an additional feeding
source for sandflies, which increases contact between vec-
tors and humans. Improved housing protects against vec-
tor-borne diseases, since it reduces human-vector
exposure. Reported household use of a mosquito net was
associated with increased risk of ACL scar, which may
reflect the practice of selling insecticide-treated nets at
highly subsidized prices to refugee households with active
ACL.

Although parasite identification was not carried out in
this study, that \( L. \) tropica is the etiologic agent seems prob-
able because it causes most leishmaniasis cases in Central
Asia (5,10), and transmission is characterized by cluster-
ing of cases and higher risk among children. Our data indi-
cate that parasite transmission is autochthonous in
surveyed sites, although highly heterogeneous between
sites. Observed childhood-acquired immunity indicates
that not all cases are imported from Afghanistan, as has
been suggested (5). Consequently, continual and vigilant
surveillance is required to monitor the epidemiology of
ACL in the region. The mass return of \( Leishmania\)-infec-

DISPATCHES
ed refugees to urban areas in Afghanistan poses a particular risk, since housing is often poor, and living conditions are crowded. Including ACL prevention measures in Afghanistan’s basic package of health services (e.g., supplying insecticide-treated nets to areas at high risk) should be considered to prevent the spread of disease through previously ACL-free urban areas.

Current ACL interventions in the study areas in Pakistan are funded by the United Nations High Commissioner for Refugees (UNHCR) and mainly focus on Afghan refugees. Free diagnosis on the basis of clinical symptoms, analysis of specimens by microscope, and treatment with antimony are provided for all patients attending basic health units in refugee camps, and insecticide-treated nets are sold at highly subsidized prices to refugees with active ACL. The local population is not a focus of the program, since resources are limited. Insecticide-treated net users in local villages either make their own nets or acquire them through “leakage” of nets intended for Afghan refugees or at communities across the

Table 1. Unadjusted odds ratios for variables associated with the risk of anthropogenic cutaneous leishmaniasis lesion and scar

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lesion [OR (95% CI)]</th>
<th>Scar [OR (95% CI)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Village</td>
<td>( \chi^2 = 540, \text{ df } = 66, \text{ p } &lt; 0.001 )</td>
<td>( \chi^2 = 786, \text{ df } = 66, \text{ p } &lt; 0.001 )</td>
</tr>
<tr>
<td>Refugee camp (compared to local village)</td>
<td>1.540 (1.16–2.06), \text{ p } = 0.003</td>
<td>0.82 (0.62–1.09), \text{ p } = 0.19</td>
</tr>
<tr>
<td>Nationality (Afghan compared to Pakistani)</td>
<td>1.050 (0.78–1.38), \text{ p } = 0.720</td>
<td>0.940 (0.70–1.26), \text{ p } = 0.680</td>
</tr>
<tr>
<td>Years lived in camp/village</td>
<td>1.010 (1.01–1.02), \text{ p } &lt; 0.001</td>
<td>1.002 (0.99–1.01), \text{ p } = 0.510</td>
</tr>
<tr>
<td>Family member visited Afghanistan in last 12 mo.</td>
<td>1.740 (1.37–2.20), \text{ p } &lt; 0.001</td>
<td>1.690 (1.35–2.11), \text{ p } &lt; 0.001</td>
</tr>
<tr>
<td>Lesion prevalence in other household members</td>
<td>1.120 (1.11–1.13), \text{ p } &lt; 0.001</td>
<td>1.040 (1.03–1.06), \text{ p } &lt; 0.001</td>
</tr>
<tr>
<td>Scar prevalence in other household members</td>
<td>1.030 (1.02–1.03), \text{ p } &lt; 0.001</td>
<td>1.090 (1.08–1.10), \text{ p } &lt; 0.001</td>
</tr>
<tr>
<td>Sex (female compared to male)</td>
<td>1.010 (0.89–1.15), \text{ p } = 0.770</td>
<td>1.050 (0.95–1.16), \text{ p } = 0.310</td>
</tr>
<tr>
<td>Age group (compared to 0–4 y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5–19 y</td>
<td>1.090 (0.87–1.37), \text{ p } = 0.450</td>
<td>1.750 (1.44–2.13), \text{ p } &lt; 0.001</td>
</tr>
<tr>
<td>≥20 y</td>
<td>0.560 (0.43–0.71), \text{ p } &lt; 0.001</td>
<td>1.080 (1.07–1.59), \text{ p } = 0.007</td>
</tr>
<tr>
<td>Type of wall (compared to mud)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brick</td>
<td>0.940 (0.33–2.68), \text{ p } = 0.920</td>
<td>0.640 (0.31–1.31), \text{ p } = 0.220</td>
</tr>
<tr>
<td>Stone</td>
<td>0.530 (0.32–0.88), \text{ p } = 0.010</td>
<td>0.480 (0.30–0.77), \text{ p } = 0.002</td>
</tr>
<tr>
<td>Other</td>
<td>2.000 (0.76–5.21), \text{ p } = 0.150</td>
<td>1.160 (0.59–2.31), \text{ p } = 0.650</td>
</tr>
<tr>
<td>Type of ceiling (compared to cloth)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concrete</td>
<td>0.690 (0.26–1.79), \text{ p } = 0.450</td>
<td>1.090 (0.44–2.71), \text{ p } = 0.850</td>
</tr>
<tr>
<td>Wood (beam)</td>
<td>1.430 (0.65–3.17), \text{ p } = 0.370</td>
<td>1.590 (0.73–3.48), \text{ p } = 0.240</td>
</tr>
<tr>
<td>Wood (thatched)</td>
<td>0.460 (0.16–1.27), \text{ p } = 0.140</td>
<td>1.770 (0.70–4.49), \text{ p } = 0.230</td>
</tr>
<tr>
<td>Other</td>
<td>0.850 (0.30–2.41), \text{ p } = 0.760</td>
<td>1.180 (0.47–2.99), \text{ p } = 0.710</td>
</tr>
<tr>
<td>Rooms/person</td>
<td>0.200 (0.07–0.56), \text{ p } = 0.002</td>
<td>0.430 (0.21–0.91), \text{ p } = 0.020</td>
</tr>
<tr>
<td>Cows in compound (yes/no)</td>
<td>1.420 (1.22–1.65), \text{ p } &lt; 0.001</td>
<td>1.510 (1.34–1.69), \text{ p } &lt; 0.001</td>
</tr>
<tr>
<td>Dogs (yes/no)</td>
<td>1.660 (1.42–1.94), \text{ p } &lt; 0.001</td>
<td>1.310 (1.16–1.48), \text{ p } &lt; 0.001</td>
</tr>
<tr>
<td>Meshed windows (% windows covered)</td>
<td>1.260 (0.51–3.13), \text{ p } = 0.610</td>
<td>0.720 (0.32–1.61), \text{ p } = 0.420</td>
</tr>
<tr>
<td>Use mosquito net</td>
<td>1.180 (0.83–1.67), \text{ p } = 0.350</td>
<td>1.560 (1.19–2.05), \text{ p } = 0.001</td>
</tr>
<tr>
<td>Treated mosquito net</td>
<td>0.760 (0.32–1.78), \text{ p } = 0.530</td>
<td>0.740 (0.42–1.32), \text{ p } = 0.320</td>
</tr>
</tbody>
</table>

\( \text{OR}, \text{ odds ratio}; \text{ CI}, \text{ confidence interval}; \text{ df}, \text{ degrees of freedom}. \)

\( ^a \text{The overall significance of this categorical variable is shown rather than the 67 different survey locations.} \)

Table 2. Adjusted odds ratios associated with risk of anthropogenic cutaneous leishmaniasis lesion and scar, based on multiple logistic regression model, using village as a random effect variable

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lesion Adjusted OR (95% CI)</th>
<th>Scar Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group (compared to 0–4 y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5–19 y</td>
<td>1.17 (0.90–1.52) \text{ p } &lt; 0.001</td>
<td>2.52 (1.93–3.29) \text{ p } &lt; 0.001</td>
</tr>
<tr>
<td>≥20 y</td>
<td>0.48 (0.35–0.65) \text{ p } &lt; 0.001</td>
<td>1.99 (1.48–2.69) \text{ p } &lt; 0.001</td>
</tr>
<tr>
<td>Lesion prevalence in other household members</td>
<td>1.10 (1.09–1.11) \text{ p } &lt; 0.001</td>
<td>1.48 (1.03–2.14) \text{ p } = 0.040</td>
</tr>
<tr>
<td>Scar</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age group (compared to 0–4 y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5–19 y</td>
<td></td>
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</tr>
<tr>
<td>≥20 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refugee camp (compared to local village)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scar prevalence in other household members</td>
<td>1.08 (1.07–1.11) \text{ p } &lt; 0.001</td>
<td>1.48 (1.03–2.14) \text{ p } = 0.040</td>
</tr>
</tbody>
</table>

\( \text{OR}, \text{ odds ratio}; \text{ CI}, \text{ confidence interval}. \)
border in Afghanistan. Long-term control of ACL transmission in Pakistan will require extending diagnostic and treatment services and building up a program to sell insecticide-treated nets to the local population. With the ongoing reduction in UNHCR funding and anticipated phasing-out of support to refugee health care at the end of 2005, the population will depend on the Pakistan Ministry of Health to deliver these much needed services.

Acknowledgments

We are grateful to the HealthNet International survey team and the temporary surveyors for collecting data and Clive Davies and Paul Coleman for statistical advice and comments on the manuscript.

The HealthNet International Malaria and Leishmaniasis Control Programme in Pakistan is supported by the UNHCR, who does not accept responsibility for the information provided or views expressed. S.B. is supported by the Wellcome Trust.

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References


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