Post-earthquake outbreak of cutaneous leishmaniasis in a rural region of southern Iran

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Human cutaneous leishmaniasis (CL) is of increasing public-health importance in Iran. On 10 July 2003, two mild earthquakes struck the rural town of Zarindasht in the southern Iranian province of Fars. The results of passive detection of CL cases in this town (in which patients with any skin lesions were evaluated) from April 2002 to April 2004 indicated that the earthquakes may have led to an outbreak of the disease; annual incidence increased from 58.6 detected cases/100,000 in the 12 months before the earthquakes to (an outbreak peak of) 864 detected cases/100,000 in the following 12 months. In addition, the incidence of detected CL in the town that was struck by the earthquakes in 2003 was significantly higher in the 12 months after the earthquakes than that recorded, over the same 12 months, for Fars province as a whole ($P<0.05$). Most (70%) of the cases detected in the town were aged ≤ 10 years, about half (50.4%) of the detected skin lesions were on the face, and most (89.7%) of the skin lesions were caused by *Leishmania major*. Incidence over the study period showed marked seasonality, with most (79.5%) of the detected cases occurring between November and February. In areas where the disease is endemic, CL may need to be considered among the health threats posed by natural disasters such as earthquakes, and increased surveillance for CL after future earthquakes may be justified.

Natural disasters often have devastating impacts on the health of human populations and their livestock (Abolghasemi *et al.*, 2006). Earthquakes, for example, may demolish many buildings, leaving large numbers of people displaced and/or forced to take temporary refuge in nearby tents, usually under crowded conditions and poor standards of hygiene. In areas where vector-borne diseases are endemic, the displacement of thousands of people may dramatically increase human exposure to vectors and the pathogens that they may carry, resulting in increases in the incidence of human infection (Desjeux, 2004)

— especially if such displacement occurs when vector density is at its seasonal peak. There is, for example, evidence of post-earthquake increases in the transmission by *Phlebotomus papatasi* of *Leishmania major*, to both dogs and humans (Reithinger *et al.*, 2007; Ait-Oudhia *et al.*, 2009).

Human cutaneous leishmaniasis (CL) is still a public-health problem in many countries of the Eastern Mediterranean region, including the southern, central and eastern provinces of Iran (Asgari *et al.*, 2007; Ruiz Postigo, 2010). Although CL is, officially, a notifiable disease in Iran, declaration of detected cases is not mandatory and so the official figures on incidence usually underestimate the true burden of the disease.

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Most cases of CL in Iran are of the 'wet' zoonotic form (ZCL) caused by *L. major*, with wild rodents acting as 'reservoir' hosts in rural areas (Moemenbellah-Fard *et al.*, 2003). Fars province, in southern Iran, is a main focus of CL, with reported annual incidences of 108–144 cases/100,000 people (WHO, 2008). On 10 July 2003, a rural county town in Fars, Zarindasht, was rocked by two earthquakes, the first (measuring 5.6 on the Richter scale) occurring at 21.36 hours and the second (of magnitude 5.8) at 22.12 hours. Overall, 4519 buildings were destroyed, one person was killed and 20 injured. The main aim of the present study was to check CL incidences in Zarindasht before and after the earthquakes, to see if the earthquakes had a significant effect on the local transmission of the parasites causing the disease (i.e. *L. major* and *L. tropica*).

This is the first report from a rural area of southern Iran on earthquake-associated changes in CL. Globally, fewer than 10 articles on leishmaniasis following natural disasters have been published. In Iran, at least two attempts have been made to see if the major earthquake that hit the south-eastern city of Bam on 26 December 2003, killing >41,000 people, had a significant effect on the incidence of the 'dry' anthroponotic form of CL (ACL) found in the area. When Aflatoonian and Sharifi (2006) compared the incidence of new cases of ACL in Bam 1 year after the quake with those recorded in the 4 years before it, they found no significant difference. More recently, however, an analysis of ACL incidences over a 20-year period (1988–2007) has associated the 2003 earthquake with a six-fold increase in ACL incidence among Bam residents, as well as revealing gender- and age-related shifts in the incidence of the disease, towards men in higher age-groups (Aflatoonian and Sharifi, 2010).

SUBJECTS AND METHODS

Study Area

The study was focused on the county town of Zarindasht, which was formed, from the main

township of Hajiabad (54°25'E, 28°22'N) and five satellite villages (Dareh-Shoor, Dehen, Dabiran, Zirab and Old City), in October 2001. Zarindasht lies in an arid rural plain 280 km to the south-east of Shiraz, the capital city of Fars province, at an altitude of about 870 m above sea level. It has a hot dry climate, with a mean annual temperature of 21°C and a mean annual rainfall of 170 mm. The main occupation of the 25,000 people who live in the rural town is agriculture.

As a control, data from the county town of Darab (which, although only 70 km to the north-east, was apparently unaffected by the 2003 earthquake in Zarindasht) were also collected and analysed. Darab had a population of about 108,600 in 2004, lies at an altitude of about 1150 m above sea level, and has a mean annual temperature of 22°C and a mean annual rainfall of 272 mm.

Subjects

Active detection of CL in the residents of Zarindasht and Darab was discounted because of the logistical problems in checking people who, mostly, leave their homes early each morning and spend their days working in the surrounding fields. Any resident of either town who had one or more skin lesions and presented, between 1 April 2002 and 31 March 2004, at a clinic run by the local health authority was examined so that the cause of the skin lesion(s) could be identified (see below). Each patient aged >16 years who had skin lesions and a parent/guardian of each younger patient with such lesions was given a standardized questionnaire so that, with the assistance and under the supervision of a health officer, they could record the age, gender, place of residence and household size of each patient and the causes and clinical attributes of the patient's skin lesions.

Diagnosis and *Leishmania* Detection

After they or their parents/guardians gave informed consent, patients with CL, who

usually had lesions on the exposed skin of their face or limbs, were diagnosed clinically. The disease was then confirmed by the detection of amastigotes, under oil immersion at $\times 1000$, in an air-dried, methanol-fixed and Giemsa-stained impression smear of scrapings from the nodular margins of a lesion. The ZCL caused by *L. major* (and usually found in rural areas) was distinguished from ACL caused by *L. tropica* (more usually found in urban areas) by measuring the size of the amastigotes and counting how many of them there were in each infected macrophage. Patients with amastigotes measuring 4–5 μm in diameter and with <10 amastigotes in each infected macrophage were assumed to be infected with *L. major* whereas patients with smaller amastigotes (1.5–2.5 μm in diameter) and with up to 100 amastigotes/infected macrophage were assumed to be infected with *L. tropica* (Faulde *et al.*, 2008a, b). [Although the amastigotes from only a few patients were identified to species level using PCR-based assays, in each case the species identified by examination of the smears was confirmed by the PCR (data not shown).]

Data Analysis

Data on patient age, gender, place of residence, household size and clinical attributes [date of lesion onset, location of lesion(s) on body, number of lesions and other dermatological details] from each study town were compared using Student's *t*-tests. The data collected in the 12 months beginning 1 April 2002 (before the 2003 earthquakes) and in the 12 months beginning 1 April 2004 (after the earthquakes) were compared using χ^2 tests and graphs prepared using the Excel software package (Microsoft). In some of the comparisons, the corresponding incidence data for the whole of Fars province, as reported by the Iranian Ministry of Health using the numbers of notified CL cases (unpubl. obs.), were also included.

A *P*-value of ≤ 0.05 was considered indicative of a statistically significant difference.

RESULTS

Over the 3-year study period, 1738 patients were confirmed as CL cases in the two study towns: 851 in Zarindasht and 887 in Darab (Table 1).

Pre-earthquake Demography

In the 12 months beginning 1 April 2002, the number of CL cases detected in Darab (123) was about eight-fold higher than the number recorded in Zarindasht (15) but the different populations sizes of the two towns meant that the corresponding incidences, in cases/100,000 people, were similar ($P>0.05$). Compared with the corresponding mean incidence for the whole of Fars province, however, that recorded among the residents of Darab in the same 12-month period was significantly higher ($P<0.05$).

Post-earthquake Demography

Almost all (98.24%) of the patients who presented with active skin lesions in Zarindasht after the 2003 earthquakes were confirmed as CL cases. Annual incidence of CL in this town increased from 58.6 cases/100,000 in the 12 months beginning 1 April 2002 (i.e. 'pre-earthquakes') to 491 cases/100,000 in the 12 months beginning 1 April 2003 and 864/100,000 in the 12 months beginning 1 April 2004. In the first and, particularly, the second of the 12-month study periods after the 2003 earthquakes, the incidence of detected CL in Zarindasht was significantly higher than that reported for the whole of Fars province ($P<0.05$ for each).

In the control town of Darab, only 86% of the patients who presented with active skin lesions after the 2003 earthquakes in Zarindasht were confirmed as CL cases. The annual incidence of CL in Darab rose from 60.2 cases/100,000 in the 12 months beginning 1 April 2002 (i.e. 'pre-earthquakes') to 225 cases/100,000 in the 12 months beginning 1 April 2003 and 218 cases/100,000 in the 12 months beginning 1 April 2004. After the earthquakes in Zarindasht, the mean

probability of a resident of Darab having active CL was significantly greater than the mean probability for a resident of the province of Fars ($P<0.05$) but significantly lower than the mean probability for a resident of Zarindasht ($P<0.05$). The ratio of the annual incidence of (detected) CL in Zarindasht to that in Darab (see Table 1) was about 2 in the first 12 months after the Zarindasht earthquakes and almost 4 in the second of the 12-month study periods after the Zarindasht earthquakes.

Most (88%) of the CL cases detected in Zarindasht were aged <20 years (Fig. 1) and lived in large, low-quality houses in rural areas. All age-groups were, however, affected to some extent by CL, with the youngest case in Zarindasht aged <1 year and the eldest aged >89 years (median = 11.8 years). Although more of the Zarindasht cases were female (55.8%) than male (44.2%), the incidence of CL among the female residents of the town was not significantly different from the incidence among the male residents ($P>0.05$). Most (83%) of the Zarindasht cases each lived with more than three family members.

In Zarindasht, the commonest location for a skin lesion caused by CL was the face (50.4%) and most (77.6%) of the detected CL cases had a single lesion each (Table 2). The incidence of CL over the 3-year study period showed marked seasonality, with 79.5% of the cases detected in Zarindasht occurring in the cooler months of November–February (Fig. 2). Over the same 3-year period, a similar cold-season peak was seen in the incidence of notified CL cases in Fars province as a whole (Fig. 2). On the basis of the size of the amastigotes seen in impression smears and the numbers of amastigotes seen in each infected host cell, most (89.7%) of the CL cases detected in Zarindasht were attributed to *L. major*.

DISCUSSION

Human leishmaniasis appears to be a major public-health problem in Iran, with numerous rural foci of ZCL and urban foci of ACL and more than half of the 31 Iranian provinces affected by at least one form of

TABLE 1. The numbers of cases and incidences of cutaneous leishmaniasis (CL) recorded within Zarindasht, Darab and the whole of Fars province, over the 3-year study period

Location	Year beginning 1 April:		
	2002	2003	2004
ZARINDASHT			
No. of CL cases detected	15	306	530
Incidence (cases/100,000)	58.6	491	864
Ratio of incidence:mean incidence of CL in Fars province, and (corresponding <i>P</i> -value)	1.17 (0.63)	4.68 (0.00001)	7.38 (0.00001)
Ratio of incidence:incidence of CL in Darab, and (corresponding <i>P</i> -value)	0.97 (0.97)	2.19 (0.00001)	3.97 (0.00001)
DARAB			
No. of CL cases detected	123	395	369
Incidence (cases/100,000)	60.2	225	218
Ratio of incidence:mean incidence of CL in Fars province, and (corresponding <i>P</i> -value)	1.2 (0.05)	2.14 (0.00001)	1.86 (0.00001)
FARS PROVINCE			
No. of CL cases detected	1978	4404	4944
Incidence (cases/100,000)	49.9	105	117

FIG. 1. The distribution of cutaneous leishmaniasis (CL) lesions according to the age of the case of CL, as recorded in Zarindasht over the 3-year study period.

the disease (Azizi *et al.*, 2010). Both ACL and ZCL also occur in neighbouring Afghanistan and Pakistan, where war, poor infrastructure and/or refugee migration have led to recent outbreaks (Rowland *et al.*, 1999; Reyburn *et al.*, 2003; Faulde *et al.*, 2008a, b, 2009). In areas where the disease occurs,

TABLE 2. Numbers and locations of the skin lesions seen on the cases of active cutaneous leishmaniasis detected in Zarindasht over the 3-year study period

Variable	No. and (%) cases
NO. OF LESIONS/CASE	
1	644 (77.6)
2	192 (20.6)
>2	15 (1.8)
SITE OF LESION(S)	
Face	429 (50.4)
Hand	138 (16.2)
Foot	60 (7.1)
Trunk	17 (2.0)
Other	207 (24.3)

eco-epidemiological changes, whether anthropogenically or naturally induced, may trigger increases in the incidence of CL — although such increases could be mitigated by the proper implementation of integrated preventive measures (Faulde *et al.*, 2009).

This is the first formal report from Fars province on an outbreak of CL apparently caused by earthquakes in a rural town. Although >90% of CL cases heal naturally within 3–18 months (Davies *et al.*, 2003), it is not difficult to find active cases in most regions of Fars province (Moemenbellah-Fard *et al.*, 2003; Fakoorziba and Nazari, 2006; Azizi *et al.*, 2006, 2008; Razmjou *et al.*, 2009; Davami *et al.*, 2010) and, in the present study, there was evidence of earthquake-related increases in the incidence of new CL cases more than 12 months after the earthquakes had occurred. Although, over Fars province as a whole and in a town in the province that appeared unaffected by

FIG. 2. Seasonality in the incidence of cutaneous leishmaniasis, as seen in Zarindasht (□) and Fars province as a whole (■) over the 3-year study period.

the Zarindasht earthquakes, the incidence of (detected) CL increased between 2002 and 2004, the corresponding increase recorded in Zarindasht was much greater. This observation indicates the existence of a major variable that (while having little or no effect at the provincial level) influenced *Leishmania* transmission to the human residents of Zarindasht. It is highly likely that this variable was the effect of the two earthquakes in July 2003, which, although responsible for only one death, caused immense ecological changes, disrupted the routine activities of the townspeople, and caused many residents to sleep outdoors until the threat of aftershocks and further damage to buildings had decreased. It seems very likely that the earthquake damage created many new resting and breeding sites for the sandfly vectors, while the post-earthquake behaviour of the townspeople (with residents and recovery workers removing debris, restoring housing, and living under substandard living conditions) increased their exposure to the bites of the vectors. It also seems likely that the

earthquakes displaced some of the wild mammals that act as the 'reservoir' hosts of *L. major*.

The observation that most of the CL cases detected in Zarindasht were children or teenagers probably indicates the existence of acquired immunity in the older residents of the town and, perhaps, behaviour patterns in the children (such as outdoor play) that increase their exposure to sandfly bites (Reithinger *et al.*, 2007). The present observations (in which earthquakes appear to have had a relatively quick impact on the incidence of CL) differ markedly from those made after the last major earthquake in Bam (in which the earthquake appears to have had a medium-term but not such a short-term impact on the local CL; Aflatoonian and Sharifi, 2006, 2010). The CL in Bam appears to be entirely ACL (with no rodent hosts of the causative parasites), however, whereas the CL in Zarindasht appears to be predominantly ZCL. Curiously, most of the lesions seen in Bam were on the hands and legs of the CL cases (Aflatoonian and

Sharifi, 2006, 2010), not (as in Zarindasht; present study) on the face. Areas of skin that are left uncovered when a person is clothed are easily accessible to a hungry female sandfly, especially if they are relatively soft (Lehane, 2005).

The seasonality seen in the incidence of clinical CL in Zarindasht, with 79.5% of all cases occurring in the cooler months of November–February, is similar to that reported in northern Afghanistan (Faulde *et al.*, 2008a). In the latter area, however, the incidence of ZCL was found to peak slightly earlier in the year (i.e. September–October), possibly because the ‘cold season’ starts earlier in the year in northern Afghanistan than further south, in southern Iran.

There appear to be three main causes of CL outbreaks. One is the influx of susceptible people, such as travellers and immigrants, into zoonotic foci (Desjeux, 2004). Tourists, new settlers and deployed soldiers, for example, may become involved in outbreaks when they enter an endemic area (Jumaian *et al.*, 1998; Ashford, 2000, 2001). Another cause of ZCL epidemics is the ecological changes that follow certain types of weather. Periods of rain, for example, may allow the populations of rodent ‘reservoir’ hosts and sandfly vectors to flourish and expand, increasing transmission of *L. major* to humans (Ben Salah *et al.*, 2007). A third potential cause of a CL outbreak is the introduction, by infected humans, of leishmanial parasites into a new area where potential vectors (and, in the case of *L. major*, potential reservoir hosts) are already abundant (Gramiccia and Gradoni, 2005). If *L. tropica* is the introduced parasite, the outbreak can then be supported and spread by human–vector–human transmission. All three potential causes of CL outbreaks may have contributed to the increases in CL incidence seen in post-earthquake Zarindasht.

In 2003, natural disasters contributed hugely to the disability-adjusted life-years (DALY) lost in Iran, being the second most

important cause among male Iranians of all ages and the third most important among female Iranians (Naghavi *et al.*, 2009). In the many earthquake-prone areas of the country, earthquakes may often have dramatic impacts not only on the epidemiology of many diseases (including CL, especially if it is already endemic) but also on healthcare (if the health infrastructure is severely damaged). There needs to be both greater appreciation of the health risks associated with such natural disasters and careful planning for post-earthquake disease control and surveillance.

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