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Economic Consequences of Post–Kala-Azar Dermal Leishmaniasis in a Rural Bangladeshi Community

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Abstract. Post–kala-azar dermal leishmaniasis (PKDL) is a complication of visceral leishmaniasis. Bangladesh national treatment guidelines during the study period called for 120 intramuscular injections of sodium antimony gluconate (SAG). We assessed care-seeking behavior, diagnosis and treatment costs, and coping strategies among 134 PKDL patients; 56 (42%) patients had been treated with SAG, and 78 (58%) remained untreated. The median direct cost per patient treated was US$367 (interquartile range [IQR] = 90–284), more than two times the estimated per capita annual income for the study population. The most common coping strategy was to take a loan; the median amount borrowed was US$98 (IQR = 71–150), with a median interest of US$32 (IQR = 16–95). Households lost a median of 123 work-days per patient treated. The current regimen for PKDL imposes a significant financial burden, reinforcing the link between poverty and visceral leishmaniasis. More practical shorter-course regimens for PKDL are urgently needed to achieve national and regional visceral leishmaniasis elimination goals.

INTRODUCTION

Visceral leishmaniasis is caused by protozoan parasites of the *Leishmania donovani* complex and is transmitted by sand fly vectors.[1] Clinical visceral leishmaniasis, also known as kala-azar, is usually fatal if left untreated.[1] The largest focus of visceral leishmaniasis exists in South Asia, where 200 million people are estimated to be at risk.[2] India, Bangladesh, and Nepal together account for 60% of the estimated 500,000 annual clinical cases and nearly 70% of annual deaths.[3] In this region, visceral leishmaniasis is caused by the protozoan parasite *L. donovani* and transmitted by female *Phlebotomus argentipes* sand flies. Transmission is anthroponotic in South Asia: infected humans constitute the only proven reservoir of the disease.[1]

Post–kala-azar dermal leishmaniasis (PKDL) is a complication of visceral leishmaniasis. Characterized by a macular, papular, or nodular rash, PKDL develops months to years after apparently successful treatment of kala-azar or in rare cases, in the absence of clinical visceral leishmaniasis.[4–6] At the time of study, the Bangladesh national treatment guidelines recommended 6-month-long treatment with sodium antimony gluconate (SAG) for PKDL. This regimen consists of 120 intramuscular injections (20 per month with 10-day rest periods in between each 20-day course).[7] Sodium stibogluconate is associated with a range of adverse effects, including myalgias and arthralgias, chemical and clinical pancreatitis, and in rare cases, cardiac conduction system effects that can result in death.[8] In addition to potential toxicity, such prolonged treatment raised questions about feasibility and affordability. The public supply of SAG was unstable in the country, and based on the data from kala-azar studies, the economic burden of PKDL treatment was expected to be high.[9]

There are no published empirical data on the economic burden of PKDL treatment. Such data are necessary to assess the impact of PKDL on household economy and poverty and bolster the effort to develop and validate alternative treatment regimens for PKDL. Therefore, we designed the present study to investigate PKDL care-seeking behavior and the economic impact of the current PKDL treatment regimen on affected households. In addition, we collected data on coping strategies taken by families to finance the treatment.

METHODS

Study site. The study was conducted in Fulbaria, a sub-district of the Mymensingh district in north-central Bangladesh, from September 9 to December 6, 2009. The Mymensingh district has the highest reported incidence of kala-azar in Bangladesh, and Fulbaria is the most affected sub-district.[10] This study was conducted in conjunction with an ongoing project covering eight communities selected on the basis of a high reported kala-azar incidence. Since 2007, population-based active surveillance has been conducted to measure the annual incidence of kala-azar and PKDL in the study communities.[5] All households in the study area were enumerated in 2007. Demographic information and data on history of kala-azar and PKDL were collected and updated yearly since 2007. As of December 2009, the total population under surveillance comprised 22,699 individuals from 4,553 households. The annual kala-azar incidence peaked at 85 per 10,000 in 2004 and fell to 46 per 10,000 in 2007, but PKDL incidence rose from 1 per 10,000 in 2002–2004 to peak at 21 per 10,000 in 2007.[5] Among kala-azar patients who subsequently developed PKDL, the median age at the time of kala-azar onset was 11 years compared with 14 years for kala-azar patients without PKDL. At the time of this study, the majority of patients received treatment at Fulbaria Upazila Health Complex, a government clinic where SAG was officially provided free of cost.

Study design. We attempted to interview all past and current PKDL patients detected by active case-finding in the ongoing surveillance project. Newly ascertained patients whose disease fulfilled the PKDL case definition were also eligible to enter the current study. A past PKDL case patient was defined as an individual with a macular, papular, or nodular rash for at least 1 month that was diagnosed by a physician and treated with SAG with resolution. A current PKDL case patient was

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defined as an individual with a macular, popular, or nodular rash for at least 1 month that was diagnosed by the study physician who was experienced in the clinical diagnosis of the disease. A minority of PKDL cases had laboratory confirmation by a polymerase chain reaction (PCR) method, which was described in a previous publication.[5] The only treatment for PKDL available in Bangladesh at the time of study was SAG. Thus, patients who received a course of SAG injections for PKDL were considered treated. Patients who never received SAG for PKDL were considered untreated.

We used a structured questionnaire to collect information on care-seeking behavior (i.e., number of healthcare provider visits and type of provider) and household costs incurred through activities related to the diagnosis and treatment of PKDL. The questionnaire was adapted from an earlier study on the economic impact of kala-azar conducted in the same study area.[9] In addition, we collected information on coping strategies, such as sales of assets and loans. Clinical status, treatment history, and demographic data were updated as necessary based on the same questions used during the routine active surveillance updates. We administered the questionnaire to the PKDL patient or a member of the household who served as a caretaker and could provide the relevant information. All interviews were conducted in Bengali. Data entry errors were checked against completed questionnaires.

Ethical approvals. The study protocol was reviewed and approved by the ethical review committees of the International Center for Diarrheal Disease Research, Bangladesh (ICDDR,B) and the Centers for Disease Control and Prevention (CDC). We obtained written informed consent from the adult study participants in each household before administering the questionnaire. Written informed consent was obtained from the parents or guardians of children included in the study; assent was also obtained from children 7 years or older.

Analysis. Data were analyzed using Stata version 10.1 (StataCorp LP, College Station, TX). To identify factors that influenced care-seeking behavior of PKDL patients, we constructed univariate and multivariable models with the outcome of interest as treated for PKDL. The variables examined included sex, age (both as a continuous variable and categorized by 5-year intervals) at first PKDL symptom onset, calendar year of symptom onset, aerial distance from the patient's residence to the Fulbaria Upazila Health Complex, whether the patient was ever told to get injections, whether the patient was ever given the diagnosis of PKDL, village, number of months from kala-azar treatment to PKDL onset, and whether the patient had antecedent kala-azar. We postulated these variables *a priori*. Based on information obtained during the course of the study, we dichotomized the calendar year of symptom onset into two categories (2002–2006 and 2007–2009). We chose 2007 as the cutoff, because a new PKDL referral guideline was introduced in the study area that year. Before 2007, Upazila Health Complex physicians could make a clinical diagnosis of PKDL and begin treatment based on their diagnosis. The new guideline instituted in 2007 recommended that Upazila Health Complex doctors refer possible PKDL patients to the district hospital (approximately 30 km outside the study area) for a confirmatory diagnosis based on slit skin smear and treat them only if the district hospital recommended treatment. Sex and age at PKDL onset were not significantly associated with the outcome in univariate analyses, but they were considered as potential confounders and included in the multivariable model.

Economic impact was assessed by estimating the total household cost per treated patient. We grouped direct expenditure into four categories: diagnosis, treatment, transportation, and miscellaneous costs. The diagnosis cost included formal provider fees and the cost of any tests performed for PKDL diagnosis. The treatment cost consisted of the cost of SAG, other medications, and syringes plus informal fees or gifts to medical personnel who administered SAG injections. The monetary value of gifts was estimated by interviewees. The cost of SAG, normally provided free of charge at Upazila Health Complex, was included, because a number of patients reported having to purchase vials from local markets when the Upazila Health Complex supply was insufficient. Transportation cost included expenses for the patient and those people who accompanied the patient. The miscellaneous cost consisted of the cost of special food given to PKDL patients and any other expenses incurred to the household because of PKDL treatment. Special foods included more expensive items often prioritized for those people thought to require special nutritional attention (e.g., sick or pregnant household members). The most common special foods included eggs, milk, chicken, bananas, apples, and oranges.

We also considered three additional types of cost associated with PKDL treatment: lost productivity because of missed work days, lost earnings because of temporary transfer of assets, and loan interest. To estimate lost productivity, we first identified household members (the patient or those people who accompanied the patient) who missed work days because of PKDL diagnosis and/or treatment. Then, we determined the average daily income of each person at the time when work-days were missed and how many days were lost. In the study area, two types of loans were common: conventional loans with a specific rate of interest and loans in which some of the borrower's assets are temporarily transferred to the lender. In the latter case, a borrower transfers goods or property (usually a piece of farm land or a cow) to the lender until the loan principal is fully paid; the income generated from the asset during the loan period is kept by the lender and lost by the asset's owner. We considered interest charged on a monetary loan and lost earnings because of temporary transfer of assets separately. When a household had multiple cases of PKDL with overlapping treatment periods and expenses, we estimated per patient cost by taking an average for each expense category. All expenses and costs were converted to 2009 value using annual inflation rates and were expressed in US dollars (US$) at the exchange rate of 1 US$ = 70 taka.[11]

RESULTS

Study participants. We interviewed a total of 134 PKDL patients, 61 females (46%) and 73 (55%) males. The population for this analysis included 125 (92%) of 136 PKDL patients ascertained before data collection plus 9 additional patients detected during this fieldwork; 11 patients were not available for interview. Fifty-six (42%) patients had been treated for PKDL, and 78 (58%) patients were untreated (Table 1). Only 22 (28%) of 78 patients with PKDL onset between 2007 and 2009 had been treated compared with 34 (61%) of 56 patients with onset between 2002 and 2006 ($P < 0.001$). The median age at PKDL symptom onset was 13 years (interquartile range

TABLE 1
Characteristics of persons with PKDL in Fulbaria, Bangladesh in 2009

	Treated (*N* = 56; 42%)	Untreated* (*N* = 78; 58%)	Total (*N* = 134)	*P* value†
Demographic status				
Age at PKDL (years)				
Median	13.5	13.5	13	0.43
Range	3–58	2–54	2–58	0.43
Female (%)	52	41	46	0.22
Clinical status				
Current PKDL status (%)				
Resolved	50 (89)	22 (28)	72 (54)	< 0.001
Not resolved	6 (11)	56 (72)	78 (46)	< 0.001
Symptom onset year (%)				
2002–2006	34 (61)	22 (28.2)	56 (41.8)	< 0.001
2007–2009	22 (39.3)	56 (71.8)	78 (58.2)	< 0.001
Disease duration‡ (months)				
Median	12.5	19	14	0.029
Range	3–54	2–40	2–54	0.029
Access to care				
Distance to Upazila Health Complex§ (km)				
Mean	4.97	6.38	5.78	0.001
Standard deviation	2.56	2.37	2.54	0.001
Visited any health provider (%)	56 (100)	27 (34.6)	83 (62.0)	< 0.001
Visited Fulbaria Upazila Health Complex (%)	52 (92.9)	22 (28.2)	74 (55.2)	< 0.001
Total number of visits¶				
Median	3	0	1	< 0.001
Range	1–15	0–8	0–15	< 0.001

* Patients who never received sodium antimony gluconate (SAG) treatment of PKDL.
† *P* values were determined by two-sample Wilcoxon rank sum test for age, total number of visits, and disease duration, two-sample *t* test for distance to the Fulbaria Upazila Health Complex, and Pearson's χ^2 test for other variables.
‡ From PKDL onset to resolution. Median values were estimated for patients who recovered and whose onset and resolution dates were available (i.e., 46 treated, 19 untreated, and 65 total).
§ Minimum distance in kilometers from a patient's house to the Fulbaria Upazila Health Complex.
¶ The total number of visits to any health provider before initiating treatment.

[IQR] = 9–21). There was no significant difference in age ($P = 0.43$) distribution between treated and untreated patients. In the univariate analysis, females were more likely to have received treatment than males, but this association did not reach statistical significance ($P = 0.22$); 62 patients (6 treated and 56 untreated) had skin lesions at the time of interview. A total of 72 patients (50 treated and 22 untreated patients) reported complete resolution of PKDL. Of 56 treated patients, 45 patients completed the 120-injection course, 10 patients stopped treatment early, and 1 patient was undergoing treatment at the time of interview.

Of 134 participants, 83 (62%) patients had visited at least one health provider seeking a diagnosis. The Fulbaria Upazila Health Complex was the most common site of first consultation (74%) followed by village doctors (11%) and private clinics (8%). Village doctors usually have no formal training but are recognized by their communities as healthcare providers. Seventy-four patients (55% of 134) were examined at least one time at the Fulbaria Upazila Health Complex for PKDL. Patients reported a median of three visits (IQR = 1–4.5) to providers before beginning SAG treatment. Of 78 untreated patients, 51 patients (65%) did not seek medical assessment for the condition. Untreated patients who reported any visits to health providers made a median of two visits (IQR = 1–4).

In the final multivariable model that included sex, age at PKDL symptom onset, calendar year of symptom onset, and distance from the patient's house to the Fulbaria Upazila Health Complex, all variables but age at PKDL symptom onset were strongly associated with receipt of SAG treatment (Table 2). Those patients who developed PKDL between 2007 and 2009 had 74% lower odds (95% confidence interval [CI] = 43–88%) of having received treatment compared with those patients with onset in 2002–2006. Patients who lived farther from the Upazila Health Complex were also less likely to have received treatment: for every 2-km increase in distance, the odds of receiving treatment decreased by 36% (95% CI = 14–53%). We observed a significant association between patient's sex and final treatment status after adjusting for year of symptom onset and the distance to the Upazila Health Complex. In the final model, male patients were less likely than females to have received treatment, and this association reached statistical significance (57% lower odds of receiving treatment, 95% CI = 5–81%). There was no significant interaction between the variables sex and distance or sex and calendar year.

TABLE 2
Crude and adjusted relative odds of receiving SAG for PKDL

	Crude		Full model*	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Sex				
Female	1.0	–	1.0	–
Male	0.65 (0.32, 1.29)	0.22	0.43 (0.19, 0.95)	0.037
Age at PKDL†	1.0 (0.98, 1.03)	0.69	1.00 (0.97, 1.03)	0.97
PKDL onset year				
2002–2006	1.0	–	1.0	–
2007–2009	0.25 (0.12, 0.53)	< 0.001	0.26 (0.12, 0.57)	0.001
Distance to Upazila Health Complex‡	0.64 (0.48, 0.85)	0.002	0.64 (0.47, 0.86)	0.004

OR = odds ratio; CI = confidence interval.
* Multiple logistic regression model including all variables listed.
† Odds ratios estimated for every 1-year increase in age.
‡ Odds ratios estimated for every 2-km increase in distance.

Household economic impact. Of 56 treated patients, one patient was a military officer with treatment costs entirely covered by the government; data from this patient were excluded from the economic analysis. The median total direct expenditure per treated patient was US$179 (Table 3). The

TABLE 3
Expenditure because of treatment with SAG

Type of expenditure	Mean (SD)*	Median (IQR)*	Proportion of total expenditure (%)†	*n*‡
Diagnosis	6 (9)	5 (0, 8)	3.0	41
Provider fee	0.4 (1)	0 (0, 0)	0.2	10
Test	6 (9)	5 (0,127)	2.8	38
Treatment	56 (66)	27 (15, 65)	25.6	54
SAG	24 (54)	0 (0, 12)	11.1	22
Other medication	18 (31)	5 (0, 21)	8.3	40
Syringe	8 (4)	8 (6, 11)	3.8	53
Informal payments to providers	5 (6)	4 (1, 7)	2.3	42
Transportation	53 (55)	44 (11, 73)	24.3	49
Miscellaneous	103 (116)	69 (30, 137)	47.1	49
Special food	101 (117)	66 (28, 137)	46.4	49
Other miscellaneous	2 (10)	0 (0, 0)	0.7	3
Total	218 (170)	179 (90, 284)	100	55

SD = standard deviation; IQR = interquartile range.
* Values were the mean or median of 55 patients who received SAG treatment. One patient, who was a military officer and whose expenditures were entirely covered by the government, was excluded from the analysis. Values are expressed in 2009 US dollars after adjusting for inflation.
† Proportion of mean total expenditure because of each category of expense.
‡ The number of individuals (among the 55 patients) who reported expenditure for the particular category.

cost of providing special food comprised the biggest proportion followed by treatment and transportation costs. In comparison, diagnosis cost was low. Of 55 treated patients, 42 (84%) patients made informal payments to providers who administered injections, either in cash or in the form of gifts such as sweets. Although SAG is normally provided at no cost at the Fulbaria Upazila Health Complex, 40% of treated patients reported having to purchase some or all treatment drug. Treated patients used a variety of strategies to minimize treatment-related costs. Common strategies included sharing a vial of SAG between PKDL patients, walking partway or the entire way to the Upazila Health Complex, sharing transportation with other patients, and minimizing the quantity of special food purchased for the patients.

Of 55 treated patients, 48 (87%) patients reported that their treatment resulted in decreased household assets because of lost income, temporary transfer of assets, and/or loan interest payments. The median asset loss per treated patient was US$170 (Table 4). Lost income comprised the largest proportion; each PKDL treatment course resulted in a median of 43 lost days. Many patients reported being accompanied by a female household member, most of whom were homemakers whose lost time was not included in the monetary estimates of lost income. When these lost work days were included, the median days lost per treated patient increased to 123 days or more than one-third of 1 year.

Combining direct expenditure and lost household economic assets, the median total household cost per treated patient was US$367 (IQR = 90–284) with a mean of $677 (standard deviation [SD] = 1,125). The total cost of untreated PKDL was substantially lower; 58 of 78 untreated patients (74%) reported no direct expenditures. Only one untreated patient took a loan with interest to cover the cost of care provided by a traditional healer.

Coping strategies. Of 55 treated patients, 45 (82%) patients reported that their households used at least one type of coping strategy to finance PKDL treatment. The most commonly used strategies consisted of loans (60%) followed by sale of assets (45%) (Table 5). Thirteen treated patients (24%) reported making temporary asset transfers as collateral for loans, resulting in income loss. In all cases, transferred assets were farm land for rice cultivation. A total of 34 households, consisting of 33 households with treated patients and 1 household with an untreated patient, took at least one loan with interest. These households borrowed a median of US$98, with a median interest (accrued and paid as of the date of interview) of US$32 or nearly one-third of the median principal (Table 6); 23 households reported borrowing from one source, 9 households reported borrowing from two sources, and one household reported borrowing from three sources. The most common loan source was a neighbor followed by relatives and microcredit lenders.

Table 4

Costs because of lost productivity, other lost earnings, and/or loan interest associated with treatment

Category	Mean (SD)*	Median (IQR)*	Proportion of total costs (%)	n†
Lost income caused by lost work	402 (981)	90 (0, 391)	87.6	41
Lost income caused by rental assets	18 (47)	0 (0, 0)	3.9	13
Loan interest payment	39 (78)	5 (0, 49)	8.5	29
Total	459 (1,001)	170 (32, 450)	100	48

SD = standard deviation; IQR = interquartile range.

*Values were the mean or median of 55 patients who received SAG treatment. One patient, who was a military officer and whose expenditures were entirely covered by the government, was excluded from the analysis. Values are expressed in 2009 US dollars after adjusting for inflation.

†The number of individuals (among the 55 patients) who reported expenditure for the particular category.

Table 5

Coping strategies taken by households with treated PKDL patients

Strategy	n (%)*
Sale of assets	25 (45)
Rental of assets	13 (24)
Loans	33 (60)
Any of the three strategies	45 (82)

*The proportion of the 55 treated patients whose household reported a particular coping strategy (Tables 3 and 4). The values add up to more than 100%, because a number of households used multiple coping strategies.

DISCUSSION

At the time of our study, most PKDL patients in Bangladesh did not seek treatment, and those people who did encountered many barriers. These barriers included the cost of transportation, special diets, and sometimes, treatment drug, but perhaps most importantly, they included the many days of lost income resulting from the prolonged regimen. Despite this finding, most patients who started treatment had the persistence and hardiness to complete the full 120-injection course. Some barriers came from the healthcare system itself. Before 2007, Fulbaria Upazila Health Center physicians were able to prescribe PKDL treatment without further referral, but beginning in 2007, new guidelines required patients to obtain a recommendation for treatment from the district hospital (30 km from the Upazila Health Center). Despite the good intentions behind promoting a stricter requirement for PKDL diagnosis, this change seems to have discouraged many PKDL patients from seeking treatment.

Because PKDL patients are usually not systemically ill, why is PKDL treatment important? PKDL has been known to be infectious to sand flies since 1928.[12] Patients with PKDL, particularly the nodular forms, are known to remain infectious for decades, and they are thought to provide a durable infection reservoir that allows transmission to be sustained when kala-azar incidence is driven to very low levels, which it was by widespread indoor residual spraying during the 1950s and 1960s.[13,14] Because kala-azar patients are usually treated within a few months of symptom onset, their contribution to the overall infection reservoir may be less than

Table 6

Source, principal, and interest of loan taken by PKDL households

Source	n	Principal (in US$)*		Interest (in US$)*	
		Mean (SD)	Median (range)	Mean (SD)	Median (range)
Neighbors	15	105 (81)	81 (15–324)	44 (42)	32 (0–120)
Relatives	14	88 (78)	78 (6–284)	37 (61)	11 (0–194)
Microcredit	8	148 (142)	113 (33–486)	83 (165)	18 (3–486)
Cooperative	6	73 (24)	85 (28–90)	51 (33)	47 (17–106)
Bank	2	85 (14)	75–95	15 (5)	15–11
Overall	34	136 (119)	98 (6–486)	64 (91)	32 (0–486)

SD = standard deviation.

*Median and mean values were estimated with the denominator equal to n for each category. Values are expressed in 2009 US dollars after adjusting for inflation.

that of PKDL patients who remain untreated for years. Untreated PKDL patients, therefore, threaten the basic feasibility of eliminating visceral leishmaniasis as a public health problem.

Visceral leishmaniasis has strong bidirectional links with poverty.[9,15–22] In South Asia, endemic foci are concentrated in rural areas and poorer states, and highly affected communities seem to be poorer than other communities in the same district.[16,19] Superimposed on this background, the disease itself further impoverishes affected families. For example, the median treatment cost for a kala-azar patient exceeded the median per capita annual income by 20% in the earlier Bangladesh study.[9] In Nepal, expenditures for treatment of visceral leishmaniasis caused 20% of previously non-poor study households to fall below the national poverty line.[16] Our study shows the even greater financial burden caused by PKDL in Bangladesh. We estimate that the median annual per capita income in the study site was approximately US$160 based on income data collected in the same population in 2004 adjusted for growth in the Gross Domestic Product (GDP) in Bangladesh between 2004 and 2009.[11] This finding implies that the median per patient cost for PKDL treatment was greater than the annual per capita income of the study population.

Because most PKDL occurs in treated kala-azar patients, nearly every household affected by PKDL must bear more than one heavy financial burden within a few years—first for kala-azar and then for PKDL treatment. Successive needs for costly treatment in a relatively short time frame may be catastrophic to affected families, many of who already live in poverty. One mother lamented her inability to provide her son with any additional food at the time that he was undergoing treatment. She reported that four earlier cases of kala-azar in the family had exhausted all their cash reserves, and by the time that the boy developed PKDL, they no longer had any valuables that could be sold or rented. For families like hers, the only available source of funds is a loan with a high interest rate.

These observations are consistent with findings from low-income countries with limited formal health insurance coverage. In Asian countries like Bangladesh, China, India, Nepal, and Vietnam, families manage more than 60% of healthcare costs out of pocket.[23] Large out of pocket health expenditures alone can exacerbate poverty.[23] More importantly, strategies that families use to cope with an illness can deplete assets, cause long-term indebtedness, and have a catastrophic impact on household welfare.[24–26] Economists define health spending as catastrophic when a household spends a large fraction of the household budget at the expense of its subsistence.[27,28] In our study, when lost income and debt payments were taken into account, the total expenditure for 86% of treated patients exceeded the median per capita income. Thus, PKDL treatment is likely to lead to catastrophic health expenditure for the majority of affected households.

The current study also found that patients were less likely to seek care for PKDL if they lived far from the provider or were required to be evaluated first at the district hospital. In particular, after the new referral guideline was introduced in 2007, PKDL patients seem to have been discouraged from seeking further medical attention because of logistical and financial constraints. Adding to the economic burden of the prolonged treatment, these barriers to healthcare access affect the disease outcome of individual patients and may have lead to low treatment uptake in the study population. In the present study, nearly 60% of all PKDL went untreated, and these patients had PKDL symptoms (and therefore, might be hypothesized to be infectious to sand flies) for a median of 25 months when they were interviewed for this study. Data from the active surveillance project showed a sharp increase in PKDL incidence in 2007 and 2008, echoing the prior kala-azar epidemic that peaked in 2005.[5] Given the lack of active PKDL surveillance and sensitive diagnostic testing, the low treatment uptake leading to an increasing cumulative burden of untreated PKDL translates to a persistent and growing parasite reservoir in the community. These barriers to care may, therefore, have the unintended consequence of increasing levels of leishmaniasis transmission in the community.

Our study had several limitations. First, we relied primarily on recall by patients and/or their family members for an illness that occurred as early as 2003. Although we obtained written records of treatment and associated costs whenever possible, inaccurate recall may have caused under- or overestimation of the strength of associations and expenditure estimates. However, the requirement of 120 injections and trips to a hospital is a major family event that is not easily forgotten. Indeed, many of our interviewees remembered and described their experiences and expenses in impressive detail. Second, the difficulty of achieving parasitological diagnosis of PKDL may have resulted in over- or underdiagnosis in the study population. Diagnosis of PKDL is currently largely clinical, because the available tests, such as microscopic or molecular examination of a slit skin sample or skin biopsy, require invasive sampling and have suboptimal sensitivity, especially in macular disease.[6] Clinical diagnosis can be subjective, especially by physicians without PKDL experience and in mild disease. In the present study, those patients who reported that their lesions resolved after 120 injections were considered as having past PKDL, and we have no way of determining the validity of their diagnoses that were made at local health facilities. In addition, our clinical data were insufficiently quantified to determine how the severity of PKDL lesions and changes in severity may have affected care-seeking behavior and resulting treatment-related expenses. It is also possible that the questionnaire may not have captured all categories of treatment-related costs. Finally and most importantly, our data did not include household-level assessment of income and other socioeconomic indicators, which may have had an impact on the ability to pay for care.

Conditions that influence treatment costs and the likelihood of receiving treatment vary among visceral leishmaniasis-endemic areas within Bangladesh and across the region. Qualitative studies are necessary to better capture the social and economic implications of PKDL. Thus, the generalization of our results to other populations should be made with caution. Nevertheless, the present study underscores the extremely high cost of the prolonged PKDL treatment regimen in endemic communities. Consistent with previous studies of the economic impact of kala-azar in South Asia, we found the overall cost of treatment to be substantially greater when associated costs, such as informal payments to service providers, lost incomes, and debt payments, are taken into account.[16,26,29] These findings clearly indicate that the treatment regimen of 120 SAG injections is neither practical

nor affordable. When a family chooses to have a PKDL patient treated, the patient will experience prolonged morbidity, and the household may be plunged further into poverty. When a family chooses not to have a PKDL patient treated, other family members and neighbors are exposed to ongoing parasite transmission.

The regional initiative to eliminate visceral leishmaniasis in South Asia was launched in 2005 with a goal of reducing the annual kala-azar incidence to below 1 per 10,000 persons by 2015.[2] However, without better treatment of PKDL, this ambitious goal is unlikely to be achieved in the near future. There is an urgent need for sensitive low-cost diagnostic tools to facilitate community-based PKDL case detection and more practical shorter-course treatment regimens. The development of such diagnostic tools and treatment regimens requires additional studies, including trials to assess the efficacy of existing and newer drugs of interest. One trial in India suggested that 12 weeks of miltefosine might provide an alternative, and liposomal amphotericin (30 mg/kg total dose administered over 3 weeks) is currently being used off-label to treat PKDL in Fulbaria.[30,31] However, further clinical trials to assess long-term efficacy of these regimens are needed. National and regional visceral leishmaniasis elimination will only be possible with coordinated efforts among stakeholders to develop and implement these tools.

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REFERENCES

1. Jeronimo S, de Queiroz Sousa A, Pearson R, 2006. Leishmaniasis. Guerrant RL, Walker DH, Weller PF, eds. *Tropical Infectious Diseases: Principles, Pathogens and Practice*, 2nd Ed. Philadelphia, PA: Churchill Livingstone, 1095–1113.
2. World Health Organization Regional Office for South-East Asia, 2009. *Kala-azar*. Available at: http://www.searo.who.int/EN/Section10/Section2163.htm. Accessed March 10, 2010.
3. World Health Organization, 2008. *The Global Burden of Disease: 2004 Update*. Geneva, Switzerland: World Health Organization.
4. el-Hassan AM, Ghalib HW, Zylstra E, Eltoum IA, Ali MS, Ahmed HM, 1990. Post-kala-azar dermal leishmaniasis in the absence of active visceral leishmaniasis. *Lancet 336:* 750.
5. Rahman KM, Islam S, Rahman MW, Kenah E, Ghalib CM, Zahid MM, Maguire J, Rahman M, Haque R, Luby SP, Bern C, 2010. Increasing incidence of post-kala-azar dermal leishmaniasis in a population-based study in Bangladesh. *Clin Infect Dis 50:* 73–76.
6. Zijlstra EE, Musa AM, Khalil EA, el-Hassan IM, el-Hassan AM, 2003. Post-kala-azar dermal leishmaniasis. *Lancet Infect Dis 3:* 87–98.
7. Thakur CP, Kumar K, 1990. Efficacy of prolonged therapy with stibogluconate in post kala-azar dermal leishmaniasis. *Indian J Med Res 91:* 144–148.
8. den Boer ML, Alvar J, Davidson RN, Ritmeijer K, Balasegaram M, 2009. Developments in the treatment of visceral leishmaniasis. *Expert Opin Emerg Drugs 14:* 395–410.
9. Sharma AD, Bern C, Varghese B, Chowdhury R, Haque R, Ali M, Amann J, Ahluwalia IB, Wagatsuma Y, Breiman RF, Maguire JH, McFarland DA, 2006. The economic impact of visceral leishmaniasis on households in Bangladesh. *Trop Med Int Health 11:* 757–764.
10. Bern C, Chowdhury R, 2006. The epidemiology of visceral leishmaniasis in Bangladesh: prospects for improved control. *Indian J Med Res 123:* 275–288.
11. International Monetary Fund, 2009. *World Economic Outlook Database, October 2009*. Available at: http://www.imf.org/external/pubs/ft/weo/2009/02/weodata/index.aspx. Accessed February 24, 2010.
12. Shortt H, Swaminath CS, 1928. Note on dermal leishmanoid. *Indian J Med Res 16:* 239–240.
13. Addy M, Nandy A, 1992. Ten years of kala-azar in West Bengal, Part I. Did post-kala-azar dermal leishmaniasis initiate the outbreak in 24-parganas? *Bull World Health Organ 70:* 341–346.
14. Sen Gupta PC, Mukherjee AM, 1968. Recurrence of kala-azar associated with post-kala-azar dermal leishmaniasis. *J Indian Med Assoc 50:* 1–5.
15. Adhikari SR, Maskay NM, 2003. The economic burden of kala-azar in households of the Danusha and Mahottari districts of Nepal. *Acta Trop 88:* 1–2.
16. Adhikari SR, Maskay NM, Sharma BP, 2009. Paying for hospital-based care of kala-azar in Nepal: assessing catastrophic, impoverishment and economic consequences. *Health Policy Plan 24:* 129–139.
17. Ahluwalia IB, Bern C, Costa C, Akter T, Chowdhury R, Ali M, Alam D, Kenah E, Amann J, Islam M, Wagatsuma Y, Haque R, Breiman RF, Maguire JH, 2003. Visceral leishmaniasis: consequences of a neglected disease in a Bangladeshi community. *Am J Trop Med Hyg 69:* 624–628.
18. Alvar J, Yactayo S, Bern C, 2006. Leishmaniasis and poverty. *Trends Parasitol 22:* 552–557.
19. Boelaert M, Meheus F, Sanchez A, Singh SP, Vanlerberghe V, Picado A, Meessen B, Sundar S, 2009. The poorest of the poor: a poverty appraisal of households affected by visceral leishmaniasis in Bihar, India. *Trop Med Int Health 14:* 639–644.
20. Meheus F, Boelaert M, Baltussen R, Sundar S, 2006. Costs of patient management of visceral leishmaniasis in Muzaffarpur, Bihar, India. *Trop Med Int Health 11:* 1715–1724.
21. Rijal S, Koirala S, Van der Stuyft P, Boelaert M, 2006. The economic burden of visceral leishmaniasis for households in Nepal. *Trans R Soc Trop Med Hyg 100:* 838–841.
22. Thakur CP, 2000. Socio-economics of visceral leishmaniasis in Bihar (India). *Trans R Soc Trop Med Hyg 94:* 156–157.
23. van Doorslaer E, O'Donnell O, Rannan-Eliya RP, Somanathan A, Adhikari SR, Garg CC, Harbianto D, Herrin AN, Huq MN, Ibragimova S, Karan A, Ng CW, Pande BR, Racelis R, Tao S, Tin K, Tisayaticom K, Trisnantoro L, Vasavid C, Zhao Y, 2006. Effect of payments for health care on poverty estimates in 11 countries in Asia: an analysis of household survey data. *Lancet 368:* 1357–1364.
24. Flores G, Krishnakumar J, O'Donnell O, van Doorslaer E, 2008. Coping with health-care costs: implications for the measurement of catastrophic expenditures and poverty. *Health Econ 17:* 1393–1412.
25. Leive A, Xu K, 2008. Coping with out-of-pocket health payments: empirical evidence from 15 African countries. *Bull World Health Organ 86:* 849–856.

26. Alamgir NI, Naheed A, Luby SP, 2010. Coping strategies for financial burdens in families with childhood pneumonia in Bangladesh. *BMC Public Health 10:* 622.
27. Wyszewianski L, 1986. Financially catastrophic and high-cost cases: definitions, distinctions, and their implications for policy formulation. *Inquiry 23:* 382–394.
28. Xu K, Evans DB, Kawabata K, Zeramdini R, Klavus J, Murray CJ, 2003. Household catastrophic health expenditure: a multicountry analysis. *Lancet 362:* 111–117.
29. Killingsworth JR, Hossain N, Hedrick-Wong Y, Thomas SD, Rahman A, Begum T, 1999. Unofficial fees in Bangladesh: price, equity and institutional issues. *Health Policy Plan 14:* 152–163.
30. Musa AM, Khalil EAG, Mahgoub FA, Hamad S, Elkadaru AMY, El Hassan AM, 2005. Efficacy of liposomal amphotericin B (AmBisomeH) in the treatment of persistent post-kala-azar dermal leishmaniasis (PKDL). *Ann Trop Med Parasitol 99:* 563–569.
31. Sundar S, Kumar K, Chakravarty J, Agrawal D, Agrawal S, Chhabra A, Singh V, 2006. Cure of antimony-unresponsive Indian post-kala-azar dermal leishmaniasis with oral miltefosine. *Trans R Soc Trop Med Hyg 100:* 698–700.