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Risk Factors for Clinical Leptospirosis from Western Jamaica

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Abstract. A retrospective, matched case-control study was conducted in Jamaica's Western Regional Health Authority (WRHA). Forty-three individuals developing clinical leptospirosis between January 2005 and December 2007 (i.e., cases) were age and neighborhood matched to 89 controls. Odds ratios (OR) and associated 95% confidence intervals (CIs) and the relative excess risk due to interaction (RERI) were calculated. Cases had increased odds of contact with rodents OR 3.52, goats OR 3.38, and being engaged in outdoor labor OR 5.30. Knowledge of leptospirosis and indoor work was protective, OR 0.39 and OR 0.16, respectively. Positive RERI values were noted for joint exposure to rodents and goats (RERI 5.54), outdoor labor and goats (RERI 6.97), and outdoor labor and rodents (RERI 30.59). Our results suggest a synergistic effect of occupational and environmental exposures on clinical human leptospirosis from the WRHA. Knowledge of the disease and its risk factors allows for protection from the disease.

INTRODUCTION

The infectious disease caused by a pathogenic species of the *Leptospira* bacteria, leptospirosis, is considered the most widespread zoonotic disease in the world, potentially affecting millions of people each year.[1–3] The World Health Organization (WHO) estimates yearly incidence rates from 1/100,000 endemically, rising to 100/100,000 during outbreaks in tropical climates, compared with 0.1–1/100,000 in temperate climates.[4] In the Caribbean, incidence rates are the highest in the world[5] and case fatality rates as high as 23.6% have been observed.[2] Due in part to the often non-specific clinical presentation and lack of diagnostic capabilities, leptospirosis is often undiagnosed or misdiagnosed.[4,6,7]

Humans become exposed to the *Leptospira* organism by contact, either directly or indirectly, with urine from infected animals. Among the more important animal sources of human exposure are rats,[7,8] horses, goats, cows, pigs, and dogs.[9,10] Dogs may contribute significantly to human exposure, particularly in tropical countries.[11] Exposure may also occur through occupational pursuits or from environmental sources such as standing water or soil containing the *Leptospira* organism.[4,7,12]

Human leptospirosis was first confirmed in Jamaica in 1953.[13] By the mid-1960s, the number of Jamaicans with antibodies to the *Leptospira* bacteria was estimated between 50,000 and 100,000.[14] Several studies consider Jamaica as having one of the highest incidence rates in the Caribbean,[15] if not the world.[5] In addition to humans, in Jamaica goats, horses, pigs, cattle, dogs, sheep, rodents, and the mongoose have all been found seropositive.[14] Despite the long history of the disease on the island and the presence of seropositive reservoirs, few published reports detail the risks for human exposure. The main aim of this study is to identify the risk factors associated with contracting leptospirosis in four western parishes of Jamaica.

METHODS

A retrospective matched case-control study of clinical leptospirosis from the Western Regional Health Authority (WRHA) of Jamaica was conducted from January 2005 to December 2007. The WRHA, one of Jamaica's four regional health authorities, serves over 464,000 people at 84 health-care centers and four hospitals in Jamaica's Western Parishes. Four parishes constitute the WRHA, including Hanover, St. James, Trelawny, and Westermorland. This study received ethical approval from the Institutional Review Board (IRB) of the University of Alabama at Birmingham, the Advisory Panel of Ethics and Meidico-Legal Affairs from the Jamaican Ministry of Health (MOH), and the WRHA.

Study population. Cases were defined as individuals who were hospitalized between January 2005 and December 2007 with serologically confirmed leptospirosis and resided in one of the four parishes served by the WRHA. Fatal leptospirosis cases from the study period were excluded from the study for accuracy of measuring exposures. Serological diagnosis was by either an immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA) (Diagnositc Automation Inc., Calabasas, CA) or a rapid IgM dot-ELISA dipstick test (DST) (PanBio Diagnostics, Queensland, Australia). Each test detected antibodies to the cross-reactive *Leptospira biflexa* patoc 1. Only individuals with test results of three full dots (strong positive) from the DST or a titer of 1:640 and above for the IgG ELISA was included in the analysis. Both tests are capable of detecting antibodies to several serovars and the DST has showed high sensitivity and specificity particularly during the acute phase.[16,17] A symptomatic patient with positive results by either of these methods is considered to have clinical leptospirosis by the Jamaica MOH. Controls were matched (1:n) to cases on neighborhood and age (±10 years). Controls were individuals without reported clinical leptospirosis, who resided in the same neighborhood as a case during the study period. Up to three controls were selected for convenience by the interviewers and interviewed on the same day as the case interview.

Data collection and statistical analysis. Data collection was conducted from May 2008 to August 2008. An in-home interviewer-administered questionnaire was conducted for both cases and controls to collect exposure information. Cases were only questioned about possible exposures from the 3 months preceding his or her leptospirosis diagnosis. Controls were questioned about possible exposures corresponding to the same 3 months as the matched case. Information gathered included occupation, animal contacts, highest education level, and behavioral habits such as walking barefoot and environmental factors such as home flooding history.

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Odds ratios (OR) and 95% confidence intervals (CIs) were calculated to measure the association between potential risk factors and clinical leptospirosis using conditional logistic regression. Relative excess risk due to interaction (RERI) was calculated for significant results. Relative excess risk due to interaction measures the additional risk experienced as a result of joint exposures.[18] The recommended reporting of interactions is to report each effect separately then the combined effects compared with the unexposed group.[19] This method allows one to use the unexposed group as a reference group to evaluate interaction on both an additive and multiplicative scale.

RESULTS

Of the 77 clinical human leptospirosis cases from the WRHA, residences were available for 50. Three of the 50 were fatal cases of leptospirosis and excluded from the analysis. Suitable controls could not be obtained for four cases, resulting in a total of 43 cases matched (1:n) to variable numbers of a total of 89 controls. Cases were mostly male (79.1%) and had a mean age of 37.8 years. Similar to cases, the majority of controls were male (62.9%) (conditional logistic OR = 5.15, 95% CI = 1.14–23.37, $P = 0.03$) and the overall mean control age was 38 years (Table 1). With regard to animal contact, cases were more likely than controls to have contact with rodents, OR = 3.52 (95% CI = 1.33–9.36, $P = 0.01$) and goats OR 3.38 (95% CI = 1.24–9.06), $P = 0.02$) (Table 2). Significant findings were noted in two occupational groups. Indoor work (healthcare, clerical, culinary, and those working from home) was protective with an OR 0.16 (95% CI = 0.04–0.71, $P = 0.02$) and outdoor labor (farming, masonry, fishing) increased the odds of disease, OR = 5.30 (95% CI = 1.41–19.92, $P = 0.01$). None of the environmental/behavioral variables were significant. Analysis of the educational variables found that knowledge of leptospirosis was protective OR 0.39 (95% CI = 0.16–0.93, $P = 0.03$), and a non-significant trend of higher OR associated with lower levels of education (Table 2). Table 3 illustrates that the relative excess risk for those engaged in outdoor labor and those who had contact with goats or rodents, and those exposed to rodents and goats exceeded the sum of each singular risk factor.

TABLE 1

General demographic information for clinical leptospirosis among cases and age-matched neighborhood controls from the Western Regional Health Authority

	Cases $N = 43$	Controls $N = 89$
Age (years)		
0–19	7	14
20–29	10	20
30–39	7	19
40–49	8	10
50–59	5	16
60+	6	10
Average age	37.84	38
Gender		
Males	34	56
Females	9	33
Parish		
Hanover	17	41
St. James	7	10
Trelawny	12	27
Westmoreland	7	11

Thirty-two of the cases were positive by the DST, 15 by the IgG ELISA, and four of the seven tested by both tests were dually positive. Three individuals whose test results did not correlate were each positive for the IgG and negative for the DST. A separate unadjusted analysis was conducted on only those testing positive by the DST with the presence of overgrown vegetation around the home OR = 4.51 (95% CI = 1.23–6.52, $P = 0.02$) and sex OR = 3.69 (95% CI = 0.77–17.63, $P = 0.10$) being the only variables with a change in significance. The ORs for the DST only sub-analysis for the other significant findings were 6.96 (95% CI = 1.96–24.78), 4.51 (95% CI = 1.42–14.28), 5.75 (95% CI = 1.51–21.86), 0.08 (95% CI = 0.10–0.64), and 0.37 (95% CI = 0.14–1.00) for contact with rodents, goats, outdoor occupations, indoor occupations, and the knowledge of leptospirosis, respectively.

DISCUSSION

In this retrospective case-control study from Western Jamaica, those with clinical leptospirosis were more likely to have one or more of the following: exposure to rodents, contact with goats, and employment in occupations involving outdoor labor. Those with the disease were less likely to have knowledge of the disease and to be engaged in indoor occupations such as culinary, clerical, or healthcare. This represents the first evidence of the protective effects of leptospirosis educational efforts in Jamaica.

The association with rodent exposure and outdoor labor occupations is expected. Rats are an important reservoir host for pathogenic serovars of *Leptospira* and the most common source for human leptospirosis.[7] Additionally, rodents have been documented as carriers of the bacteria in many Caribbean nations[15] and exposure to rodents was found to increase the odds of disease 8-fold in Barbados.[20] Similar to contact with rodents, the association between occupations involving outdoor labor and developing human leptospirosis is well documented.[7] Numerous reports from the Caribbean have documented those working in outdoor labor or farming as having the highest seroprevalence rates.[21,22] Although finding goats as contributing to human disease was not expected, it is not unreasonable. In Barbados, contact with goats was found to increase the odds of developing the disease almost 2-fold[21] and a study from Jamaica found 62% of the goats positive for *Leptospira* antibodies.[23] One of the more important findings, with respect to public health impact, was that knowledge of leptospirosis is protective. This perhaps provides evidence for the value of public health education in the region. Unlike studies in other Caribbean areas, exposure to dogs, gardening, walking barefoot, and home flooding were each non-significant.

Unlike previous studies investigating risk factors for human leptospirosis, we also explored the role of interactions among significant exposures. Positive RERI values were noted in three separate categories, 1) individuals with a combined exposure to rodents and goats, 2) employment as an outdoor laborer with exposure to goats, and 3) employment as an outdoor laborer with exposure to rodents. Exposures to these combinations of risk factors produces an amplified effect compared with what one would expect based on exposure to either risk factor. As this study was largely exploratory, RERI values were not calculated for every possible combination of interaction. Furthermore, RERI values for protective measures are difficult to interpret,[19] thus were not calculated.

TABLE 2

Univariate and multivariate analysis for matched odds ratios (OR) of clinical leptospirosis from environmental, occupational, and animal exposures

Risk factors by category	Matched unadjusted OR	*P* value	Matched adjusted OR*	*P* value
Environmental/behavioral†				
Home flooded	0.31 (0.06–1.53)	0.15	0.24 (0.05–1.29)	0.10
Participate in fresh water activities (canoe, fish, swim)	1.12 (0.44–2.83)	0.81	0.60 (0.22–1.67)	0.33
Work in garden	0.64 (0.25–1.64)	0.35	0.62 (0.29–1.60)	0.32
Knowledge of leptospirosis	0.37 (0.16–0.89)	0.03	0.39 (0.16–0.93)	0.03
Presence of overgrown vegetation around the home	1.86 (0.75–4.62)	0.18	2.22 (0.87–5.68)	0.10
Occupational†				
Unemployed	0.50 (0.12–2.07)	0.34	0.56 (0.13–2.42)	0.44
Student	1.44 (0.34–6.11)	0.62	1.38 (0.31–6.20)	0.67
Domestic work	1.40 (0.33–6.01)	0.65	2.44 (0.51–11.71)	0.26
Outdoor labor (farming/masonry/fishing)	6.73 (1.84–24.63)	< 0.01	5.30 (1.41–19.92)	0.01
Indoor non-labor	0.14 (0.03–0.62)	< 0.01	0.16 (0.04–0.71)	0.02
Animal Contact†				
Dogs	0.61 (0.27–1.41)	0.25	0.54 (0.23–1.23)	0.14
Cats	0.69 (0.26–1.82)	0.45	0.75 (0.28–2.05)	0.58
Cows	1.34 (0.34–5.26)	0.68	1.16 (0.29–4.58)	0.84
Pigs	1.87 (0.57–6.07)	0.30	1.52 (0.41–5.48)	0.52
Goats	3.59 (1.33–9.39)	0.01	3.38 (1.24–9.06)	0.02
Rodents	3.43 (1.30–9.07)	0.01	3.52 (1.33–9.36)	0.01
Chickens	1.27 (0.45–3.61)	0.65	1.07 (0.37–3.04)	0.90
Education				
University	Ref	–	Ref	–
Some Secondary	2.00 (0.68–5.58)	0.20	1.76 (0.59–5.22)	0.31
Primary	3.43 (0.96–12.26)	0.06	2.63 (0.70–9.91)	0.15
Some primary	4.23 (0.97–18.58)	0.06	2.83 (0.60–13.56)	0.19
None	0.50 (0.05–4.69)	0.55	0.47 (0.05–4.46)	0.51
Frequency of walking outside barefoot				
Less than 1 day per week	Ref	–	Ref	–
1 day per week	1.07 (0.27–4.33)	0.92	1.03 (0.26–4.13)	0.96
2–7 days per	0.23 (0.04–1.24)	0.09	0.26 (0.05–1.36)	0.11
7 days per week	0.31 (0.09–1.09)	0.07	0.36 (0.10–1.30)	0.12
Frequency of walking outside in sandals				
Less than 1 day per week	Ref	–	Ref	–
1 day per week	1.40 (0.43–4.51)	0.57	1.28 (0.37–4.48)	0.70
2–7 days per	2.27 (0.40–13.03)	0.33	1.75 (0.30–10.13)	0.53
7 days per week	2.97 (0.82–10.74)	0.10	2.72 (0.74–9.96)	0.13

*Adjusted for sex.
†Each exposure is not mutually exclusive; the unexposed group is the reference for the exposed.

The results of this study may have been affected by several limitations. The length of time between time of disease and interview may have caused a general problem of remembering exposure to possible risk factors. However, such recall bias would be non-differential misclassification thus biasing the results toward the null. Cases were diagnosed by one of two serological methods. Several studies have showed prolonged elevated anti-*Leptospiral* antibody levels.[24–27] Thus, higher titer cut-off levels are recommended for endemic areas such as Jamaica.[7] A higher cut-off was used for the IgG test in an effort to detect current disease rather than past exposure. It should be noted that each of the cases were hospital patients with symptomatic disease highly suggestive of leptospirosis and when possible other diseases with non-specific febrile symptoms were tested and ruled out. In addition, the Jamaica MOH considers a positive result from either of these tests as confirmatory for clinical leptospirosis in symptomatic patients. It is possible the MOH method misclassifies some previously exposed individuals as current clinical cases. In this situation misclassifying the individual with persistently elevated IgM would not depend on any of the exposure variables and would be considered non-differential misclassification. Controls were not randomly but conveniently selected from the same neighborhoods as the cases. Using neighborhood controls ensured selection was from the same source population as cases and it would not be unreasonable to assume conveniently selected neighborhood controls would behave differently from randomly selected ones. Interviewers knew the disease status of the interviewee, raising the possibility of introducing interviewer effects by asking probing questions differently for cases

TABLE 3

Relative excess risk caused by interactions calculated from unadjusted odds ratios (ORs) with those unexposed to both variables serving as the reference group

		Outside labor	
		+	–
Contact with goats	+	14.17	2.54
	–	4.69	1
RERI 6.94			
		Outside labor	
		+	–
Contact with rodents	+	44.11	4.35
	–	10.17	1
RERI 30.59			
		Contact with rodents	
		+	–
Contact with goats	+	9.94	2.56
	–	2.84	1
RERI 5.54			

*RERI = relative excess risk due to interaction.

than controls. The small sample size and matched design limited power to detect significant findings among variables with larger OR. Finally, although attempts were made to recruit all 77 cases identified, only 43 were actually recruited. Similarities or differences of the excluded cases to the recruited cases cannot be determined.

In summary, our results suggest clinical human leptospirosis from the WRHA is a result of occupational, environmental, and animal exposures. Deviations from additivity exist for interactions of several exposures. Such deviations suggest important synergistic effects of several risk factors in producing clinical leptospirosis. Knowledge of the disease and its causes allows for protection from the disease, perhaps providing support for the effectiveness of regional public health campaigns.

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