Human leptospirosis in the Caribbean, 1997–2005: characteristics and serotyping of clinical samples from 14 countries

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Suggested citation Adesiyun AA, Baboolal S, Suepaul S, Dookeran S, Stewart-Johnson A. Human leptospirosis in the Caribbean, 1997–2005: characteristics and serotyping of clinical samples from 14 countries. Rev Panam Salud Publica. 2011;29(5):350–7.

ABSTRACT

Objective. *To determine the frequency of human leptospirosis in the sera of suspected clinical cases sent by 14 Caribbean countries for diagnosis to a regional laboratory in 1997–2005.*

Methods. *All serum samples were initially tested using the immunoglobulin M (IgM) enzyme-linked immunosorbent assay (ELISA) for leptospirosis. Demographic data (such as age and sex), month of the year and clinical manifestations that had been observed by the attending physician were related to seropositivity. The microscopic agglutination test (MAT) was used to serotype sera using a panel of 23 international serovars.*

Results. *Of 3 455 samples tested, 452 (13.1%) were seropositive for IgM antibodies to leptospirosis by the ELISA, with frequencies significantly ($P < 0.05$; χ^2) different across countries and years. Among seropositive patients, the frequency of detection of leptospirosis (23.1%) was significantly higher in the age groups 1–20 years and 31–40 years combined compared with other age groups; and in male patients (72.1%) compared with female patients (19.7%) ($P < 0.05$; χ^2). Chills, jaundice, vomiting, weakness, diarrhea, and kidney failure/problems were significantly ($P < 0.05$; χ^2) exhibited at a higher frequency in seropositive, rather than seronegative patients. Using the MAT on 100 sera tested, 98 (98%) were seropositive, of which the serogroup Icterohaemorrhagiae was most prevalent with the detection of serovars Copenhageni (70%), Icterohaemorrhagiae (67%), and Mankarso (29%).*

Conclusions. *Since only 13.1% of the suspected cases of leptospirosis were seropositive for IgM ELISA antibodies, other clinical conditions may have been responsible for the clinical manifestations observed, or the patient may have had chronic leptospirosis (IgG). In the Caribbean, serovars of the serogroup Icterohaemorrhagiae were responsible for most infections in the cases tested.*

Key words Leptospirosis; laboratory techniques and procedures; enzyme-linked immunosorbent assay; Caribbean Epidemiology Centre; Caribbean Region.

Leptospirosis is a zoonosis of global importance and has been described as a re-emerging disease (1). Human leptospirosis has been responsible for morbidity and mortality in both developed and developing countries (2–4). Infections in humans are known to occur primarily when individuals come in contact, directly or indirectly, with urine containing viable leptospires from rodents, or by ingestion of contaminated food or water (5). Several factors, such as age, sex, season, geographical location, and occupation have been associated with human leptospirosis (6).

Leptospirosis can be confused with diseases such as dengue fever (in areas where both coexist) because of some sim-

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ilar clinical manifestations (7). Therefore, the possibility of over- or under-diagnosis of either or both conditions exists, particularly when based on clinical diagnosis only.

Several serological diagnostic methods (8–10) have been described for human leptospirosis, but the two commonly-used serological tests are the microscopic agglutination test (MAT) (8) and the enzyme-linked immunosorbent assay (ELISA) (9). The MAT is the "gold standard" for the detection of leptospiral infection, and is the most widely used method for detecting both immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies to *Leptospira* (11). The test can be used qualitatively and quantitatively to detect the infecting serovars (8) and is highly specific; however, MAT requires the propagation of live leptospiral strains, is time-consuming, and has been shown to have a low sensitivity (12). On the other hand, the ELISA involves the use of whole-leptospiral antigen preparations to screen for infection, has the ability to detect IgM and IgG antibodies separately, and is highly sensitive. Also, the fact that this assay uses killed leptospires reduces the risk of infection among laboratory personnel.

In the Caribbean, human leptospirosis has been reported in Barbados, Grenada, Guadeloupe, Jamaica, and Trinidad and Tobago (13–17). Most recently, a study (18) described serological detection of leptospirosis among patients diagnosed with dengue fever in Jamaica and there was a retrospective study in Trinidad and Tobago (19). Leptospirosis has also been recently reported in canine, rodent, and livestock populations in Trinidad and Tobago (20).

The Caribbean Epidemiology Center (CAREC) is a regional, diagnostic, reference laboratory for human diseases, including leptospirosis. Serum samples of suspected clinical cases of human leptospirosis are sent by regional and national health care facilities to CAREC for confirmation of diagnosis and for epidemiological investigation of epidemics. At the CAREC laboratory, the IgM ELISA is routinely used for the diagnosis of human leptospirosis, but serotyping of infecting leptospires is not done. Demographic information is collected for most samples submitted to the laboratory. The current laboratory-based study was, therefore, conducted to: determine the frequency of antibodies to *Leptospira* spp. in sera of suspected clinical cases of human leptospirosis submitted to CAREC; identify any associations among demographic factors (age, sex, country of origin), clinical manifestation exhibited by the patient, and season of the year, with laboratory diagnosis of leptospirosis; and determine the prevalent serovars in selected ELISA-positive sera using the MAT.

MATERIALS AND METHODS

This was a laboratory-based study that used serological tests to confirm clinical diagnosis of human leptospirosis across the Caribbean during a 9-year period. The study analyzed data to detect associations among laboratory-diagnosed leptospirosis, demographic data, and the clinical manifestations observed.

Serum samples

Serum samples originating from 14 countries during a 9-year period (1997–2005) were available for the study. These samples had been sent to CAREC when leptospirosis was suspected and verification was required. It is difficult to ascertain if the samples submitted to CAREC were representative of all cases of suspected human leptospirosis in the area or of samples collected within each country. Only single samples, not paired sera, were available for the investigation. These samples were subject to very limited thawing and freezing once they arrived at CAREC. For each serum sample sent to CAREC for testing, most demographic data (country of origin, date of collection, age, and sex), as well as clinical manifestations exhibited by each patient, were available from the laboratory database.

All sera submitted to CAREC were initially tested for IgM antibodies to *Leptospira* using the IgM ELISA for leptospirosis. Sera that (a) were positive for IgM antibodies by the ELISA and (b) had most demographic data available were selected for serotyping by the MAT.

Detection of antibodies and serovars of *Leptospira* spp.

The procedure described for IgM ELISA (9) was used to detect IgM antibodies in sera of suspected human cases of leptospirosis submitted to CAREC. Any sample with a titer of 1:640 or higher was considered positive.

The serovars of *Leptospira* spp. were detected using the MAT. A total of 100 sera were randomly selected from among the IgM ELISA-positive samples and subjected to the MAT. The antigens used for the MAT were a panel of 23 serovars provided by the Royal Tropical Institute of the Netherlands (Koninklijk Instituut voor de Tropen, Amsterdam, The Netherlands). These antigens were: *Australis Bratislava, Autumnalis Bim, Autumnalis Autumnalis, Ballum Arborea, Ballum Ballum, Bataviae Bataviae, Canicola Canicola, Cynopteri Cynopteri, Grippotyphosa Grippotyphosa, Hebdomadis Hebdomadis, Icterohaemorrhagiae Copenhageni, Icterohaemorrhagiae Icterohaemorrhagiae, Icterohaemorrhagiae Mankarso, Mini Georgia, Panama Panama, Pomona Kennewicki, Pomona Pomona, Pyrogenes Pyrogenes, Sejroe Hardjo, Sejroe Sejroe, Sejroe Wolfii, Semaranga Patoc,* and *Tarassovi Tarassovi*. The sera were initially screened for antibodies and the positive samples were titrated following standard procedures (8). For this study, the cut-off titer for positive samples by the MAT was set at 1 : 80.

Statistical analyses

SPSS® version 15.0 (SPSS Inc., an IBM company, Chicago, Illinois, United States) was used to analyze the data. The frequency of laboratory detection of leptospirosis by the ELISA was compared according to the patient's country of origin, age, sex, and clinical manifestations, and the year and month of sampling. The Kruskal-Wallis Test was performed to analyze the relationship among years, as well as among countries. Fisher's Exact Test was performed to detect any differences in the frequencies of IgM antibodies to *Leptospira* between age groups (1–20 year age group and 31–40 year group versus groups 21–30 years, 41–50 years, and > 50 years), sex (male versus female), and possible risk factors (fever, jaundice, vomiting, body pains, weakness, and a group composed of other clinical signs), as well as seasons (wet versus dry season). For both tests alpha was set at a 0.05 significance level.

Ethical approval of study

CAREC approved the study and gave the researchers the samples requested, with the sera and data for each. The Ethics Committee of the Faculty of

Medical Sciences, University of the West Indies (St. Augustine, Trinidad and Tobago) approved the research protocol prior to study commencement.

RESULTS

Over the 9-year study period, of the total of 3 455 serum samples submitted by 14 countries, 452 (13.1%) were seropositive for leptospirosis by the IgM ELISA. All samples from Anguilla (4 samples), Cayman Islands (1 sample), and British Virgin Island (3 samples) were seronegative, while for the remaining 11 countries the frequency of laboratory-diagnosed leptospirosis ranged from a low of 8.2% (Trinidad and Tobago, 140/1 709) to a high of 60.0% (Guyana, 3/5). The differences observed between countries were statistically significant ($P < 0.05$; χ^2) using the Kruskal-Wallis Test ($P = 0.00$, degrees of freedom = 13). The frequencies of seropositivity for the other countries during the study period were as follows: Antigua and Barbuda, 10% (1/10); St. Kitts and Nevis, 11.2% (23/206); Belize, 11.8% (8/68); Suriname, 16.2% (112/693); St. Lucia, 18.0% (33/183); St. Vincent and the Grenadines, 20.3% (58/286); Grenada, 22.0% (27/123); Dominica, 24.3% (17/70); and Jamaica, 31.9% (30/94).

Overall, for the countries studied from 1997–2005, the highest frequency of detection of IgM antibodies to leptospirosis was detected in 1997 (67.3%) and the second highest (15.7%) in 2005, while for the remaining years, the frequencies were variable with no observable distinct patterns. In Grenada, Guyana, Jamaica, St. Kitts and Nevis, St. Lucia, Suriname, and Trinidad and Tobago, the peak frequencies were all detected in 1997 (Figure 1). For all countries combined, the frequency of laboratory-diagnosed leptospirosis ranged from 6.0% in 1998 to 67.3% in 1997, and the differences were statistically significant ($P < 0.05$; χ^2) using the Kruskal-Wallis Test ($P = 0.032$, degrees of freedom = 8).

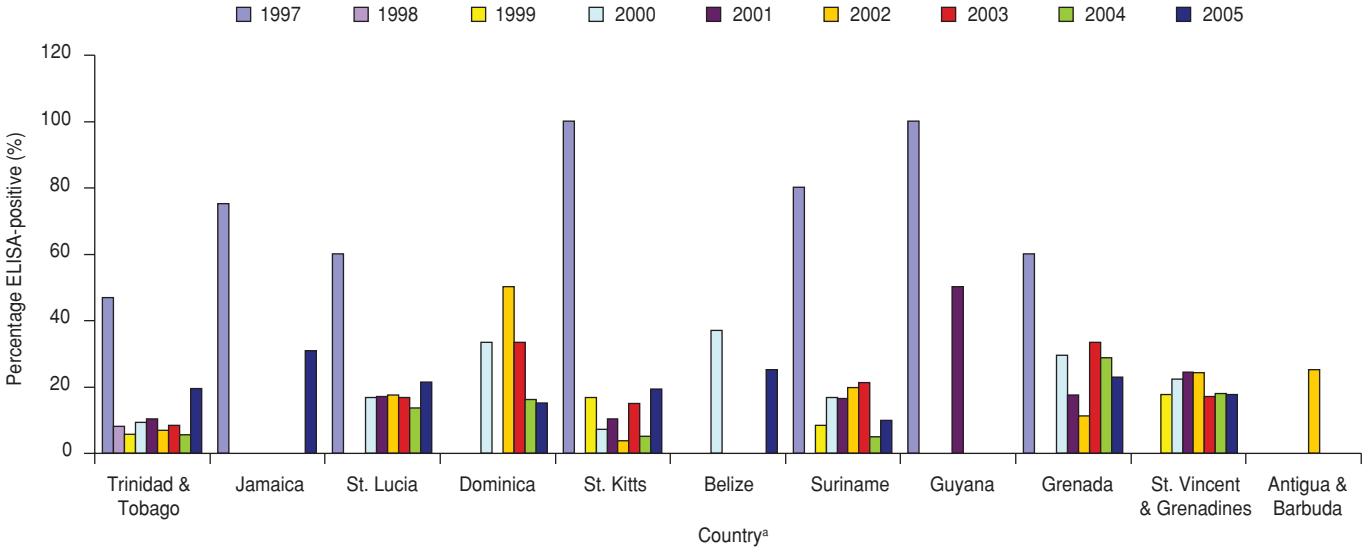
The distribution of seropositive patients by age group is shown in Figure 2. For pooled data from all countries by year of study, of the 147 IgM ELISA-positive patients with most available data, the distribution by age group was as follows: not available, 12 (8.2%); 1–20 years of age, 34 (23.1%); 21–30 years, 24 (16.3%); 31–40 years, 34 (23.1%); 41–50 years, 25 (17.0%); and > 50 years, 18 (12.2%). The highest frequency of seropositivity (23.1%) was detected in the age groups 1–20 years and 31–40 years.

For patients from all countries, the frequency of seropositive male patients (72.1%) was statistically significant ($P = 0.000$), i.e., higher than detected in female patients (19.7%); it must be noted that for 8.2% of positive patients, there was no information on the sex of the individual. Figure 3 shows that the frequency of seropositivity in males is higher than in females for all years except 1997 and 1998.

Of the 147 patients seropositive for leptospirosis by the IgM ELISA, a total of 19 clinical symptoms were exhibited, with 2–7 symptoms per patient (Table 1). Jaundice, fever, and vomiting were by far the most commonly exhibited clinical symptoms, found in 126 (85.7%), 122 (83.0%), and 87 (59.2%) patients, respectively. Jaundice was the most frequent symptom during the 9-year study period, except for in 2005 when fever was the most frequent. The frequency of clinical signs was significantly higher ($P < 0.05$; χ^2) in seropositive patients than in seronegative ones for only 6 (31.6%) of the 19 symptoms, namely, chills (36.1% versus 22.9%), jaundice (85.7% versus 57.3%), vomiting (59.2% versus 29.8%), weakness (21.8% versus 7.8%), acute diarrhea (25.2% versus 16.5%), and renal failure/problems (19.0% versus 9.2%). Frequency of fever in seropositive patients (83.0%) was not significantly higher ($P > 0.05$; χ^2) than that found in seronegative patients (76.1%).

For the period from January–May (dry season) in the Caribbean, the frequency of leptospirosis among serum samples submitted was 30.3% (40 of 132). Compared to samples from the June–December (wet season) with a rate of 45.9% (107 of 233), the difference between wet and dry season was statistically significant (P

FIGURE 1. Frequency of seropositivity for leptospirosis determined by immunoglobulin M enzyme-linked immunosorbent assay (ELISA) for 3 455 serum samples from suspected cases from 14 Caribbean countries during 1997–2005



[a] For Anguilla, the British Virgin Islands, and the Cayman Islands the percentage positive by the ELISA for all years was 0%, so these countries were not represented on the graph.

FIGURE 2. Distribution by age of 452 laboratory-confirmed cases of human leptospirosis using immunoglobulin M enzyme-linked immunosorbent assay (ELISA) on sera from 14 Caribbean countries, 1997–2005

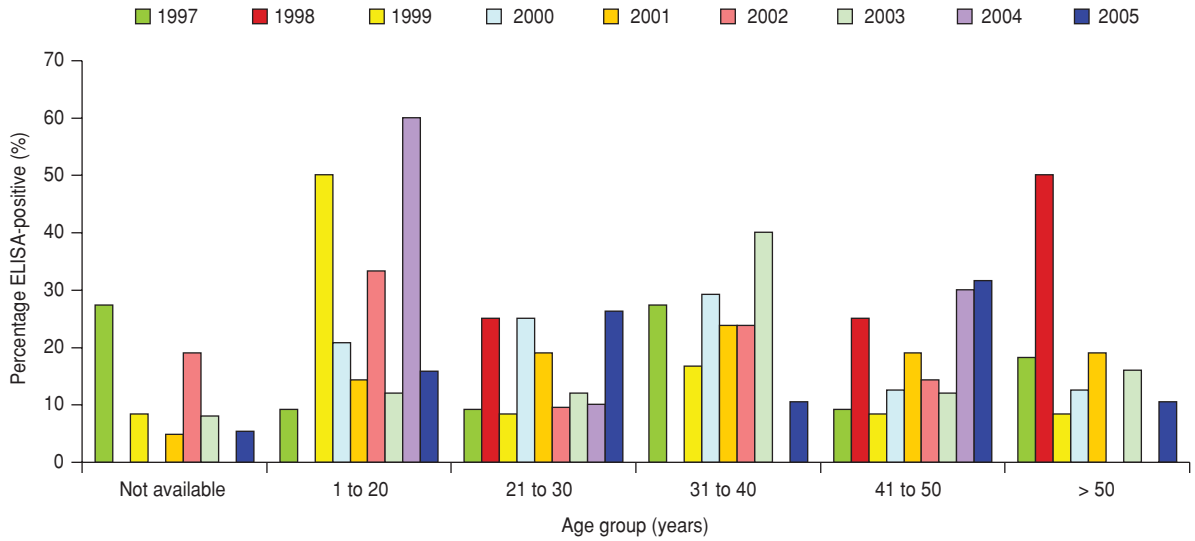
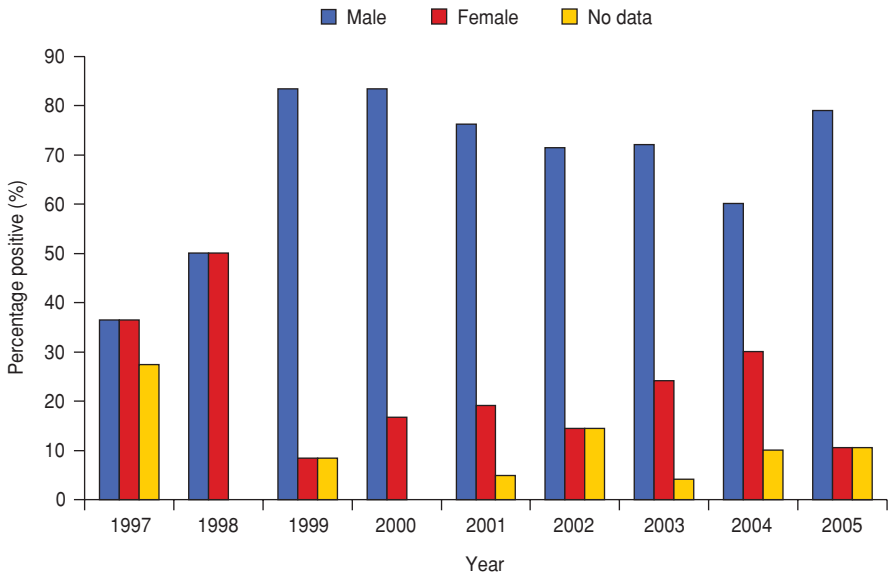


FIGURE 3. Distribution by sex of 452 laboratory-confirmed cases of human leptospirosis using immunoglobulin M enzyme-linked immunosorbent assay (ELISA) on sera from 14 Caribbean countries, 1997–2005



< 0.05; χ^2). Overall, the high frequencies of seropositivity were observed in samples submitted in December (17.0%), followed by November (12.9%) and October (9.5%) for the 9-year period. The frequency of seropositive sera by-month for each year is displayed in Figure 4, with the month of peak frequency varying considerably.

With the use of the IgM ELISA, a majority had high titers, with 33 (22.4%), 10 (6.8%), and 100 (68.0%) samples having titers of 1:640, 1 : 1280, and > 1:1 280, respectively. Of the 147 ELISA-positive samples, the distribution of titers detected were as follows: 1:80 (0.7%), 1:160 (1.4%), 1:320 (0.7%), 1:640 (22.4%), 1:1 280 (6.8%), and 1: > 1 280 (68.0%). The titer with the highest frequency among laboratory-confirmed cases of leptospirosis was 1: > 1 280 for all 9 years, with only one exception: the year 2004, when titer 1 : 640 had the highest frequency.

For the 100 sera randomly selected from the 147 ELISA-positive samples, 98 (98%) were seropositive by the MAT. Reactions were very high to serovars Copenhageni (70%), Icterohaemorrhagiae (67%), and Mankarso (29%). Forty-eight (48%) of the seropositive samples had multiple agglutinations with serovars of the Icterohaemorrhagiae serogroup, while only 5 (5.0%) had multiple agglutinations with serogroups other than serogroup Icterohaemorrhagiae. For all sera tested, serovar Icterohaemorrhagiae was most frequent during 5 years (1997, 1999, 2000, 2004, and 2005) and serovar Copenhageni, during 2 years (1998 and 2002), as shown in Figure 5.

The most detected MAT titers were 1:10240, 1: 5120, and > 1:10 240, with 47 (47%), 23 (23%), and 8 (8%) samples, respectively, accounting for 78% of all samples. Titer 1:10 240 was most frequently detected in seropositive samples, with 5 years (55.6%; 1999, 2000, 2001, 2002, and 2003) of the 9 studied, but in years 1998 and 2005, titer 1:5 120 had the highest frequency. Titers 1:2 560 and > 1:10 240 had the highest frequencies in 1997 and 2004, respectively.

DISCUSSION

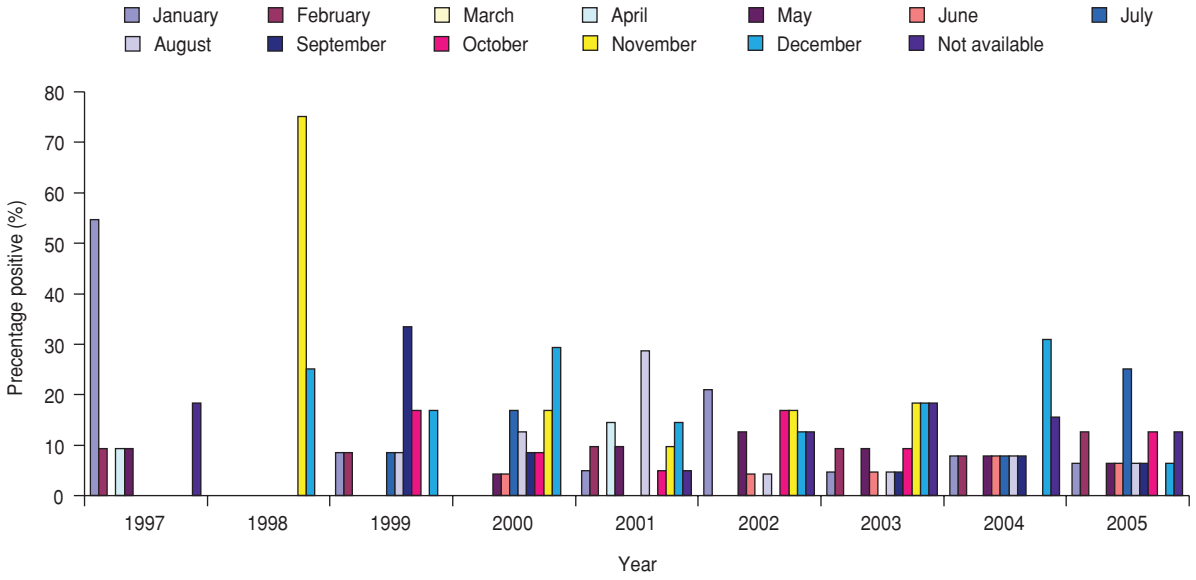
The current study covered a total of 11 (52.4%) of the 21 countries and territories in the Caribbean served by CAREC, and may be considered representative; however, the differences in the number of samples submitted by these countries cannot be ignored and may reflect the initial investigative and diagnostic activities of these countries, as well as their

TABLE 1. Frequency of commonly-exhibited clinical manifestations[a] in enzyme-linked immunosorbent assay (ELISA)-positive cases of leptospirosis from 14 Caribbean countries by year, 1997–2005

Year	No. ELISA-positive patients	Frequency of exhibition of clinical signs or symptoms							
		Jaundice (%)	Fever (%)	Vomiting (%)	Body pain (%)	Chills (%)	Dehydration (%)	Diarrhea (%)	Anorexia (%)
1997	11	8 (72.7)	8 (72.7)	3 (27.3)	4 (36.4)	1 (9.1)	4 (36.4)	2 (18.2)	4 (36.4)
1998	4	4 (100)	4 (100)	4 (100)	0 (0)	1 (25)	0 (0.0)	0 (0.0)	1 (25.0)
1999	12	10 (83.3)	9 (75)	10 (83.3)	4 (33.3)	5 (41.7)	0 (0.0)	2 (16.7)	0 (0.0)
2000	24	23 (95.8)	19 (79.2)	14 (58.3)	7 (29.2)	10 (41.7)	5 (20.8)	5 (20.8)	3 (12.5)
2001	21	16 (76.2)	17 (81)	8 (38.1)	8 (38.1)	5 (23.8)	6 (28.6)	4 (19.0)	5 (23.8)
2002	21	17 (81.0)	18 (85.7)	12 (57.1)	9 (42.9)	7 (33.3)	9 (42.9)	8 (38.1)	6 (28.6)
2003	25	23 (92.0)	21 (84.0)	17 (68.0)	7 (28.0)	10 (40.0)	7 (28.0)	6 (24.0)	10 (40.0)
2004	10	8 (80.0)	8 (80.0)	8 (80.0)	5 (50.0)	5 (50.0)	3 (30.0)	2 (20.0)	2 (20.0)
2005	19	17 (89.5)	18 (94.7)	11 (57.9)	8 (42.1)	9 (47.4)	7 (36.8)	8 (42.1)	4 (21.1)
Total	147	126 (85.7)	122 (83.0)	87 (59.2)	52 (35.4)	53 (36.1)	41 (27.9)	37 (25.2)	35 (23.8)

[a] Other clinical signs with their frequency exhibited by patients are as follows: hepatosplemegaly, 30 (20.4%); weakness, 32 (21.8%); weight loss, 25 (17.0); renal problem/failure, 25 (17.0%); respiratory problems, 15 (10.2%); conjunctivitis, 10 (6.8%); skin rash, 9 (6.1%); altered mental state, 7 (4.8%; cardiac failure/problem, 6 (4.1%); thrombocytopaenia, 4 (2.7%); and convulsion, 4 (2.7%).

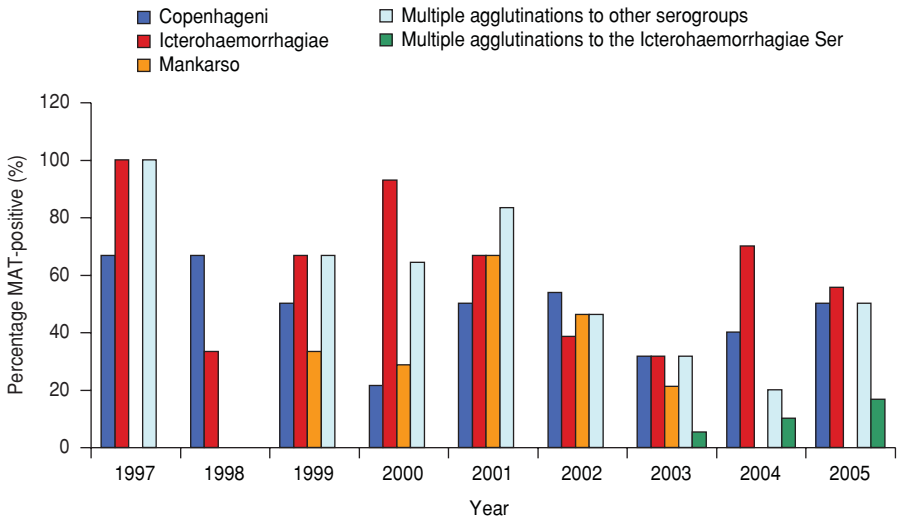
FIGURE 4. Distribution by month of the year (season) of 452 laboratory-confirmed cases of human leptospirosis using immunoglobulin M enzyme-linked immunosorbent assay (ELISA) on sera from 14 Caribbean countries, 1997–2005



reporting systems. It is possible that sample submission to CAREC was related to episodes or suspected outbreaks of human leptospirosis in these countries.

The fact that only 13.1% of the suspected cases of leptospirosis were seropositive using the IgM ELISA is an indication that a number of the cases may have been showing clinical manifestations of other conditions, such as dengue or hepatitis, which are also endemic to the area and have been reported by others (18, 21). There is also a possibility that some of the patients may have had chronic leptospirosis, and were, therefore, seropositive for IgG antibodies that were undetectable by the IgM ELISA used in this study. However, it has been reported that titers of both IgG and IgM antibodies remain for years in cases of leptospirosis (22). The diagnostic procedure used in the current study may be considered a limitation because it tested for IgM and IgG in a single sample,

FIGURE 5. Distribution by infecting serovars of *Leptospira* spp. detected by the microscopic agglitination test (MAT) in 100 randomly-selected sera from 147 immunoglobulin M enzyme-linked immunosorbent assay (ELISA)-confirmed cases of human leptospirosis from 14 Caribbean countries, 1997–2005



rather than paired samples from each patient; moreover, the time elapsed between the onset of symptoms and sampling was unknown.

The range of frequency for detection of IgM antibodies by the ELISA was from 8.2% (Trinidad and Tobago) to 60.0% (Guyana), but the frequencies in 13 of 14 countries were lower than those reported by investigators in other countries, such as Barbados, 46.7% (9) and Brazil, 94% (10) among hospitalized suspected cases of leptospirosis. Although no specific pattern was detected during the 9-year period among the countries studied, the peak frequency of seropositivity for IgM antibodies was recorded in 1997. This finding may reflect the possibility of underreporting and infrequent reporting of leptospirosis in the Caribbean. It is also possible that if there was a leptospirosis epidemic suspected in any one country, there would tend to be a cluster of suspect cases submitted by other countries to CAREC, which would affect leptospirosis detection frequency. Changes in the frequency of detection of IgM antibodies over the years have, however, been reported by others, and these have been attributed to changes in weather conditions, among other factors (4, 23).

Overall, cases of leptospirosis among those 1–20 years of age and 31–40 years of age had a significantly higher frequency of seropositivity than other age groups, a finding comparable to published reports by others (24). It has been documented that certain occupations, such as farming, sanitation/sewer work, and other activities performed by those in these age groups increase potential exposure to leptospirosis (15, 25, 26).

Similarly, the finding that male patients had a significantly higher frequency of leptospirosis than female patients is supported by reports published elsewhere (27), including recent reports from the Caribbean (18, 19, 24). Again, the patient's sex is considered to influence the type of work performed; that is, working in sugar cane or rice fields, rearing livestock, or performing manual labor (15), work predominantly carried out by males, may have affected exposure to leptospirosis. Those who work in these areas have been reported to have higher seroprevalence and/or cases of leptospirosis than members of the general population (25, 26, 28). Since the occupation of the suspect cases of leptospirosis were not available for this study, it was not possible to match occupation with sex to attempt to directly determine the association between leptospirosis frequency and patient sex. In essence, occupation may have been a confounding factor for the effect of sex in the frequency of leptospirosis observed in the current study.

It was not unexpected that clinical manifestations—chills, jaundice, vomiting, weakness, diarrhea, and renal failure—would be significantly associated with seropositivity, since these clinical signs have been documented for the disease by others (3, 10, 13). However, contrary to published reports in which fever was consistently associated with human leptospirosis (3), in the current study, the frequency of fever in seropositive patients was not significantly different from the rate found for seronegative patients. It is possible that other conditions, such as dengue, which is endemic in the area but was not tested for in the current study, may have been responsible for the finding (18, 24, 28). Leptospirosis-positive individuals have been serologically detected in dengue-positive and dengue-negative patients who exhibited fever in the Caribbean and elsewhere (18, 24, 29). It is, therefore, imperative that physicians be cognizant of the possibility of mixed infection by leptospirosis, dengue, and other conditions, and the obvious diagnostic and therapeutic implications.

The finding of the current study, that the frequency of leptospirosis seropositivity detection among suspected cases is significantly higher during the wet season than the dry, agrees with the reports of others (4, 15, 23). Other reports (4, 12, 20, 23, 26) have found that occupational exposure to leptospirosis is higher during the rainy season, coupled with an increased exposure to rodents, an important reservoir of leptospirosis.

The generally high IgM ELISA titers (68% having titers of 1 : > 1 280 in most of the study years) were considerably higher than the diagnostic cut-off titers of 1 : 80, and indicate that these are indeed infected with leptospirosis, either alone or in combination with other conditions, possibly dengue (18, 24). Detection of high titers of IgM ELISA antibodies to human leptospirosis is supported by the reports of others (30, 31).

The finding that 98 of the 100 IgM ELISA-positive sera were also seropositive by the MAT could be due to several factors. First, the MAT used in the current study is serogroup- and serotype-specific, detects both IgG and IgM, and utilized 23 serovars of the international panel. It is possible that other serovars or serogroups, not tested for in the current study, were responsible for the two ELISA-positive but MAT-negative samples. It has been documented that the number and types of serovars and the prevalent serovars causing leptospirosis in different geographical locations affect reported seroprevalences by the MAT

(32). Second, it has been reported that the ELISA is generally a more sensitive test than the MAT (33).

In this study, serogroup Icterohaemorrhagiae, particularly serovars Copenhageni and Icterohaemorrhagiae, were most prevalent and, therefore, most likely responsible for leptospirosis across the Caribbean. Of relevance was the finding that serovar Icterohaemorrhagiae was most prevalent in 6 of the 9 years studied, while in 2 years, serovar Copenhageni was prevalent. This is indicative of changing infecting serovars in geographic areas, as reported by others (34). Serovars of the Icterohaemorrhagiae serogroup had earlier been implicated in human leptospirosis within (17, 35) and beyond the Caribbean (26). The very high MAT titers detected, as similarly found with IgM ELISA titers, also suggest that the serovars detected were, in fact, responsible for the clinical disease observed. Similar high MAT and ELISA titers for leptospirosis have been reported elsewhere (30, 31).

Considering the type of information that accompanied the samples tested, the following are limitations of the current study:

(a) Data available to the reference or diagnostic laboratory (CAREC) simply listed a number of clinical signs exhibited by each patient without an indication of the severity of suspected leptospirosis observed.
(b) No evidence was available to confirm that all suspect cases of leptospirosis were reported to the respective government laboratories in each of the countries; this is why the study emphasized laboratory findings and avoided the use of the terms "incidence" or "prevalence," but used the term "frequency of seropositivity."
(c) The time of onset of clinical manifestation of the disease in patients was frequently unavailable to CAREC.

In conclusion, the low rate of detection (13.1%) of IgM antibodies to leptospirosis by the ELISA is an indication that most of the suspected clinically-diagnosed cases of leptospirosis may have been affected by other diseases, suggesting clinical overdiagnoses of leptospirosis in the Caribbean. The differences in seropositivity for IgM antibodies for leptospirosis were significantly associated with age, sex, country of origin, clinical signs exhibited, and season of the year. It is evident that the serogroup Icterohaemorrhagiae appears to be important in causing infection (acute or chronic) by *Leptospira* spp. in the Caribbean countries studied based on its frequency in the suspected cases studied. To prevent the overdiagnosis of human clinical leptospirosis in the Caribbean, it is recommended that, in addition to requesting diagnostic serological assays (IgG and IgM) for leptospirosis, other endemic diseases, particularly dengue and hepatitis, be considered.

Acknowledgements. We thank the Director of CAREC and the Head of Laboratory Services for approving this investigation. We acknowledge the University of the West Indies' School of Graduate Studies and Research, St. Augustine, Trinidad and Tobago, for funding the research.

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Manuscript received on 14 November 2010. Revised version accepted for publication on 9 March 2011.

RESUMEN

Leptospirosis humana en el Caribe entre 1997 y 2005: características y serotipificación de muestras clínicas de 14 países

Objetivo. Determinar la frecuencia de leptospirosis humana en el suero de presuntos casos clínicos enviados por 14 países del Caribe a un laboratorio regional para la confirmación del diagnóstico entre 1997 y 2005.

Métodos. Todas las muestras de suero se analizaron inicialmente mediante el ensayo inmunoenzimático de adsorción (ELISA) para detectar inmunoglobulina M (IgM) contra *Leptospira*. Se relacionó la seropositividad con datos demográficos (como la edad y el sexo), el mes del año y las manifestaciones clínicas observadas por el médico a cargo. Se usó la prueba de aglutinación microscópica para serotipificar los sueros con un grupo de 23 serovariedades internacionales.

Resultados. De las 3 455 muestras analizadas por ELISA, 452 (13,1%) fueron seropositivas para anticuerpos IgM contra *Leptospira*, con frecuencias significativamente diferentes ($P < 0,05$; χ^2) según el país y el año. En los pacientes seropositivos, la frecuencia de detección de leptospirosis (23,1%) fue significativamente mayor en los grupos etarios de 1 a 20 años y de 31 a 40 años combinados, en comparación con otros grupos de edad; y mayor en los varones (72,1%) en comparación con las mujeres (19,7%) ($P < 0,05$; χ^2). Los escalofríos, la ictericia, los vómitos, la debilidad, la diarrea y la insuficiencia o los trastornos renales fueron significativamente más frecuentes ($P < 0,05$; χ^2) en los pacientes seropositivos que en los seronegativos. De los 100 sueros que se analizaron con la prueba de aglutinación microscópica, 98 (98%) fueron seropositivos, y entre estos el serogrupo Icterohaemorrhagiae fue el más frecuente, con detección de las serovariedades Copenhageni (70%), Icterohaemorrhagiae (67%) y Mankarso (29%).

Conclusiones. Ya que solo 13,1% de los presuntos casos de leptospirosis fueron seropositivos por ELISA para anticuerpos IgM, las manifestaciones clínicas observadas pueden haberse debido a otras enfermedades, o el paciente puede haber tenido leptospirosis crónica (con anticuerpos IgG). En los casos analizados en el Caribe, las serovariedades del serogrupo Icterohaemorrhagiae causaron la mayoría de las infecciones.

Palabras clave Leptospirosis; técnicas y procedimientos de laboratorio; prueba ELISA; centro de epidemiología del Caribe; región del Caribe.