LEPTOSPIROSIS INCIDENCE AND MORTALITY IN MALAYSIA

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Abstract. Leptospirosis is endemic in Southeast Asia, Central and South America, the Caribbean, and Oceania. Malaysia was categorized as a probable endemic country without any available data. Thus, this study was conducted to determine incidence, case fatality rate and mortality rate of leptospirosis. Leptospirosis is a notifiable disease in Malaysia since 2010 whereby probable or confirmed cases must be notified to relevant health district office. There were 3,665 and 4,457 probable and laboratory confirmed leptospirosis cases notified in 2012 and 2013, respectively. In the 2-year period, the most common age group of patients was 19 years old or less (23.3%) with male:female ratio of 2.61:1. Students consisted about 16.9% of patients, followed by agriculture-based or plantation workers (14.7%). Overall age-standardized incidence rate of leptospirosis in Malaysia for 2012 and 2013 was 29.02 per 100,000. Overall case fatality rate was 1.47% for 2-year period and overall age-standardized mortality rate was 0.45 per 100,000. Leptospirosis is an emerging public health concern in Malaysia and may pose a significant health impact and burden to the nation in the coming years if not well controlled.

Keywords: case fatality rate, incidence, leptospirosis, mortality rate, Malaysia

INTRODUCTION

Leptospirosis is caused by *Leptospira*, a spirochete 0.1 μm in diameter and 6 - 20 μm in length (Adler and de la Peña Moctezuma, 2010; Lim, 2011). Leptospirosis affects populations living in more than 3 continents, including America, Asia and Europe (Pappas *et al*, 2008).To be more specific, leptospirosis is endemic in the Caribbean, Central and South America, Southeast Asia and Oceania (Pappas *et al*, 2008). In Asia, leptospirosis was reported to have an annual incidence of 0.7 cases per 100,000 in China from 1991 to 2010 (Zhang *et al*, 2012). In Malaysia, human leptospirosis was first recognized in 1925 (Bahaman and Ibrahim, 1988) and the country was categorized as a probable endemic country without any supporting data (Pappas *et al*, 2008).

Leptospirosis can be found in wild animals but is still more prominent in domestic animals including rodents, cattle, dogs and pigs (Bahaman *et al*, 1987, Adler and de la Peña Moctezuma, 2010). Transmission from animals to humans is

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increasing as human exposure to animal increases via increasing outdoor activities, military expeditions and global travel (Pappas *et al*, 2008, Adler and de la Peña Moctezuma, 2010). One of the methods for transmission is via contact with environmental surface water contaminated with urine of chronically infected mammals (Ricaldi and Vinetz, 2006). Pathogenic leptospires that live in the proximal renal tubules of carriers are excreted in urine and contaminate soil, surface water, streams and rivers (Adler and de la Peña Moctezuma, 2010).

Humans usually manifest leptospirosis as an acute infection and never become a chronic carrier (Adler and de la Peña Moctezuma, 2010). Manifestation of human leptospirosis can vary from mild to severe, including acute febrile illness, aseptic meningitis, fulminant hepatic failure, acute renal failure, pulmonary hemorrhage and severe septic shock, with mortality rate as high as 25% if early treatment is not administered (Ricaldi and Vinetz, 2006; Hartskeerl *et al*, 2011; de Vries *et al*, 2014).

In Malaysia, leptospirosis is a notifiable infectious disease for the purpose of surveillance, prevention and control of the disease. However, there have been very limited published data on the current status of leptospirosis. The paucity of information has prompted us to look into incidence and mortality rate for leptospirosis during 2012 and 2013. In particular, we were interested to investigate the demographic profile related to leptospirosis in Malaysia.

MATERIALS AND METHODS

Case detection

Leptospirosis was gazetted as a notifiable disease in Malaysia since December 9, 2010 under the Prevention and Control of Infectious Diseases Act 1988. Under the guideline published in 2011, probable or confirmed cases of leptospirosis must be notified within 1 week to the district health office. Probable case of leptospirosis is defined as a subject with positive ELISA or any other rapid tests (Disease Control Division, 2011). Confirmed leptospirosis case is a suspected or probable case with confirmatory microscopic agglutination test (MAT), positive PCR result, positive culture or demonstration of leptospires in tissue via immunohistochemical staining (Disease Control Division, 2011).

Demography of subjects

Secondary data on notification of leptospirosis nationwide from the Zoonotic Unit, Ministry of Health, Malaysia was obtained with permission for the study. Demographic characteristics, such as age, gender, ethnicity and profession, were derived from the notification. In addition, patients' outcome was also used to generate a case fatality rate and age-standardized mortality rate of leptospirosis. Analysis was conducted using an IBM SPSS Statistics for Windows software, version 20.0 (IBM, Armonk, NY) and Microsoft Excel 2007 (Microsoft, Redmond, WA). Frequencies of demographic profiles for all patients were determined. The age-standardized rates (ASRs) for incidence and mortality were also weighted using WHO world standard population distribution (Ahmad *et al*, 2001).

RESULTS

There were a total of 3,665 leptospirosis cases notified in 2012 and the figure rose to 4,457 in 2013. Of these patients, 23.3% of the cases fell into the age group of 19 years old or less followed by age group 25 to 29 years old (13.0%), 20 to 24

Table 1
Demography of leptospirosis cases reported in Malaysia, 2012 and 2013.

Characteristics	Overall Total = 8,122 *n* (%)
Age group (years)	
<19	1,889 (23.3)
20-24	980 (12.1)
25-29	1,056 (13.0)
30-34	878 (10.8)
35-39	719 (8.9)
40-44	555 (6.8)
45-49	470 (5.8)
50-54	481 (5.9)
55-59	357 (4.4)
60-64	260 (3.2)
65-69	200 (2.5)
70-74	130 (1.6)
>75	147 (1.8)
Gender	
Male	5,869 (72.3)
Female	2,253 (27.7)
Ethnicity	
Malay	4,593 (56.6)
Chinese	590 (7.3)
Indian	486 (6.0)
Sabah Natives	494 (6.1)
Sarawak Natives	517 (6.4)
Peninsular Orang Asli	221 (2.7)
Other	95 (1.2)
Foreigner	1,126 (13.9)
Occupation	
Student	882 (16.9)
Agriculture-based or plantation	766 (14.7)
Clerical or office-based worker	705 (13.5)
Unemployed	705 (13.5)
Children under 6 years old	699 (13.4)
Self-employed	547 (10.5)
Construction worker	326 (6.2)
Technical	318 (6.1)
Healthcare staff	97 (1.9)
Factory worker	88 (1.7)
Food handler	68 (1.3)
Other	18 (0.3)
Age group (years)	
<19	17.71[a]
20-24	34.34
25-29	38.95
30-34	41.32
35-39	37.50
40-44	31.31
45-49	29.25
50-54	35.17
55-59	33.53
60-64	31.56
65-69	37.16
70-74	31.73
>75	30.66

[a]Age-specific incidence rate (per 100,000 population).

years old (12.1%) and 30 to 34 years old (10.8%) (Table 1). More than half (72.3%) of leptospirosis cases were males.

As regards ethnicity, Malay (56.6%) was the most common ethnic group among the leptospirosis patients (Table 1). The second highest (16.3%) in ethnicity was the group comprising Sarawak natives, Sabah natives and *orang asli* in Peninsular Malaysia. Another significant point to mention is that foreigners who consisted of a significant portion of the work force in agriculture and plantation also made up a considerable proportion (13.9%) of leptospirosis cases.

When the 2-year leptospirosis cases were analyzed according to their profession, students formed the highest (16.9%) group, closely followed (14.7%) by agriculture-based or plantation workers (Table 1). The other common professions among leptospirosis cases were

Table 2
Age-adjusted incidence and mortality rates of leptospirosis in Malaysia, 2012 and 2013.

Characteristics	Incidence rate (per 100,000)	Mortality rate (per 100,000)
Overall	29.02	0.45
Gender		
Male	40.36	0.59
Female	16.95	0.30
Ethnicity		
Malay	33.31	0.51
Chinese	8.99	0.08
Indian	25.06	0.30
Ethnicity by gender		
Malay		
Male	46.66	0.70
Female	19.87	0.30
Chinese		
Male	11.49	0.09
Female	6.28	0.07
Indian		
Male	35.31	0.5
Female	14.74	0.11

clerical or office-based workers (13.5%), unemployed (13.5%) and children under 6 years old (13.4%).

Age-specific incidence rate was highest (41.32 per 100,000 population) in the age group 30 to 34 years old, while the second highest (38.95 per 100,000) was age group 25 to 29 years old (Table 1). Age-standardized incidence rate for leptospirosis was 13.15 per 100,000 population in 2012, but in 2013, it rose to 15.87 per 100,000. Overall age-standardized incidence rate by gender showed that male had almost two-fold higher incidence rate compared to female in the population (40.36 *vs* 16.95) (Table 2). As for age-standardized incidence rate by ethnicity, Malays had the highest incidence rate (33.31 per 100,000 population) followed by Indian and Chinese. When age-standardized incidence rate was stratified by ethnicity and gender, male preponderance of leptospirosis cases was observed in all ethnicities.

In 2012, Melaka had the highest age-standardized incidence rate (54.94 per 100,000) for leptospirosis cases, while Johor state had the lowest age-standardized incidence rate (2.11 per 100,000). In 2013, Selangor had the highest (24.68 per 100,000) in incidence rate and the lowest rate (1.82 per 100,000) was in Johor. In general, most of other states had their overall age-standardized incidence rate ranging from 28.00 to 30.00 per 100,000 population for the 2-year duration of the survey, with an increase in incidence rate in the majority of States from 2012 to 2013 while only a minority experienced a reduction of incidence rate.

Overall case fatality rate for leptospirosis for the 2-year survey period was 1.47%. When analyzed by States, it was highest (7.69%) in Labuan followed (5.26%) by Perlis (Table 3). In this context, both of these States had a low number of leptospirosis case, thus, the death of a patient could

Table 3
Age-standardized incidence rate, case fatality rate and age-standardized mortality rate of leptospirosis according to States in Malaysia, 2012 and 2013.

State	Incidence rate[a]	Case fatality rate[a]	Mortality rate[a]
Perlis	16.46	5.26	0.88
Kedah	28.87	2.85	0.80
Pulau Pinang	14.67	2.23	0.30
Perak	30.71	0.71	0.21
Selangor	39.91	0.95	0.42
Kuala Lumpur	38.46	0.00	0.00
Negeri Sembilan	32.96	1.52	0.59
Melaka	68.64	0.55	0.40
Johor	3.93	0.76	0.02
Pahang	30.14	1.14	0.36
Terengganu	30.08	2.38	0.67
Kelantan	29.95	3.47	1.04
Sabah	30.50	2.31	0.96
Sarawak	30.87	2.07	0.63
Labuan	28.02	7.69	1.97

[a]Per 100,000 population.

contribute significantly to the case fatality rate. The overall age-standardized mortality rate was 0.45 per 100,000 population. The age-standardized mortality rate was the highest (1.97 per 100,000) in Labuan, followed by Kelantan (1.04 per 100,000).

DISCUSSION

Age-standardized incidence rate of leptospirosis in Malaysia was 13.15 per 100,000 population in 2012 and 15.87 per 100,000 in 2013. Based on these incidence rates, Malaysia is ranked in the top 20 countries with the highest incidence of leptospirosis worldwide (Pappas *et al*, 2008). Among other Asian countries Sri Lanka has an incidence rate of 54, followed by Thailand (48.9), The Philippines (4.8), Taiwan (4.1), South Korea (2.8), and Singapore (2). Bangladesh, China, India, Indonesia, Iran, Kampuchea, Lao PDR, Myanmar, Nepal, and Vietnam are probable endemic but with no data.

Age and occupation have always been closely linked to leptospirosis incidence in many countries (Ciceroni *et al*, 2000; Thorley *et al*, 2002; Zhang *et al*, 2012; de Vries *et al*, 2014). In New Zealand, leptospirosis cases were prevalent in male (90.4%) and age group 25-44 years old (56.9%), with the highest proportion of occupation being livestock farming workers (51.8%), meat processing workers (31.0%) and forestry-related occupation (1.7%) (Thorley *et al*, 2002). Diversity of gender and occupation for leptospirosis is again contributed by male predominance in occupation with high leptospira exposure risk. In Andaman Island, agriculture workers are the majority with seropositivity for leptospirosis, followed by sewage workers and animal handlers (Sharma *et al*, 2006). Our study revealed that agriculture-based workers also were one of the main contributors to leptospirosis cases.

A 20-year review in China revealed male preponderance for leptospirosis with

male-to-female ratio of 2.03:1, the majority in productive age group (10-40 years old) (Zhang *et al*, 2012). Similar results were obtained in our 2-year survey. The most probable explanation for these findings is that it is related to the nature of profession for this age group. The predominant profession of leptospirosis patients in China is farming (62.0-89.0%) (Zhang *et al*, 2012). Another possible reason for male preponderance is outdoor activities, such as farm work, that lead to higher risk of exposure to leptospire-contaminated soil and water. A review by Hartskeerl *et al* (2011) concluded that changes in agriculture land use and deforestation are triggering factors for leptospirosis.

Another important finding is the commonest age group of leptospirosis in Malaysia was those below 19 years old, the majority of whom were students and children below 6 years old (32.3%). In China, the proportion of students diagnosed with leptospirosis also is prevalent (18.0-22.0%) (Zhang *et al*, 2012). This tendency could be due to frequent outdoor recreational activities among those aged below 19 years old. Another example for outdoor activity-related exposure was a leptospirosis outbreak among "Eco-Challenge" multisport (jungle trekking, prolonged swimming and kayaking, spelunking, climbing, and mountain biking) race athletes in Sabah, Malaysia, 2000 in which 42% of 189 participants fulfilled the clinical case definition of leptospirosis, but with no death reported (Sejvar *et al*, 2003). Jena *et al* (2004) reported a leptospirosis outbreak in a village in Orissa, India where the source of infection identified is infected canal water and the attack rate is the highest in age group 6 to 15 years old and more prevalent in males.

Leptopspirosis is certainly a prominent public health threat in Malaysia and surveillance of leptospirosis is crucial in understanding its distribution and prevention. Jena *et al* (2004) stressed the importance of a surveillance system, which requires that an outbreak be detected within 4 days and that action be initiated within 24 hours to contain the spread of infection. An upsurge of leptospirosis threat in urban area will be unavoidable as rapid increase of urban population and abundance of urban slums resided by locals or immigrants in Malaysia lead to overcrowding, poor sanitation, flooding risk, poverty and abundance of animal reservoir (Lau *et al*, 2010).

The strengths of this study include its nationwide data on leptospirosis covering a 2-year period in Malaysia. To the best of our knowledge, there has been no published data on incidence and mortality rate of leptospirosis in Malaysia. One of the prominent limitations was that the notification data used was not planned for research purposes but for surveillance. Thus, the parameters available were more of demographic nature and there were no data available on the clinical aspects and source of infection. Incompleteness of collected data was another limitation in the study.

In conclusion, the study provides documented evidence that leptospirosis is an emerging public health concern in Malaysia with an incidence rate of 13.15 per 100,000 population in 2012 and rising to 15.87 per 100,000 in 2013. Leptospirosis may impose a significant health impact and a burden to the nation in the coming years if the disease is not well controlled. Appropriate intervention and control measures should be employed by relevant authorities and community to reduce leptospirosis morbidity and mortality. To this end, a few intervention steps should be employed, such as intervention at the

source of infection, transmission route and lastly at the human host level.

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