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Log-Log Plot Analysis of Hand-Foot-Mouth Disease Severity in Beijing, 2009–2010

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The log-log plot was first applied to characterize 2009 H1N1 swine influenza epidemic in different countries/regions by Yoshikura (1). He also used the log-log equation $\log Y = k\log X - k\log N_0$, which is a linear regression equation after taking X and Y logarithms, to monitor, forecast, and evaluate case-fatality rates in ongoing epidemics (2). In this equation, Y is the cumulative number of deceased cases, X is that of the infected cases, N_0 is the number of infected cases when the first death occurs, the coefficient k represents the slope of the straight line, and $k\log N_0$ is the constant. SPSS can be used to assess the linear regression equation. The resulting F and *P* indicate whether the regression equation is statistically significant or not, and the adjusted R square (R^2) can give the coefficient of determination. If the slope $k = 1$, the case-fatality rate is equal to $1/N_0$. If $k > 1$, the rate increases with the number of infections, and vice versa (1). As the infectious disease epidemic progresses or areas of prevalence change, the case-fatality rate can change along with the number of infections; thus, different log-log equations can be regressed at different times or in different areas, reflecting changes in virus strains and host populations (1–4). We used the above linear regression model to measure the relationship between the infected and severe cases of hand-foot-mouth disease (HFMD) in Beijing.

HFMD can be caused by a number of species of human enteroviruses (EV), and higher virulence may be associated with specific virus strains with stronger infectivity or higher proportions of infections from such strains. Generally, enterovirus 71 (EV71) is more aggressive and causes most of the severe cases of HFMD in Beijing. The data shows that the proportion of EV71 in Beijing has remained unchanged for several years (5), but the pathogenic spectrum of HFMD cases in 2010 compared to 2009 shifted to fewer coxsackievirus A16 (CVA16) infections and more EV71 and other EV types as well as co-infections. The difference was statistically significant ($\chi^2 = 176.946$, $P < 0.01$) (Table 1).

Figure 1A shows the log-log plot of the cumulative numbers of infected cases and severe cases in 2009 and 2010, where k was >1 in both years and N_0 in 2010 was less than in 2009. The result shows that the regression equations for 2009 and 2010 were statistically significant and both adjusted R^2 values were as high as 0.97 (Table 2). It is obvious that the severity increased with the infection number in both years, and the virus strain in 2010 showed higher virulence than that of 2009.

The log-log plot of EV71 and other EV infections in

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Table 1. Pathogenic spectrum of HFMD in 2009 and 2010, Beijing

Year	EV71		CVA16		Other EVs		Co-infection		χ^2	P
	PN	CR%	PN	CR%	PN	CR%	PN	CR%		
2009	420	34.8	634	52.6	150	12.4	2	0.2	176.946	<0.01
2010	950	41.6	716	31.3	602	26.4	17	0.7		
Total	1370	39.2	1350	38.7	752	21.5	19	0.5		

HFMD, hand-foot-mouth disease; EV71, enterovirus 71; CVA16, coxsackievirus A16; PN, positive number; CR%, constituent ratio %.

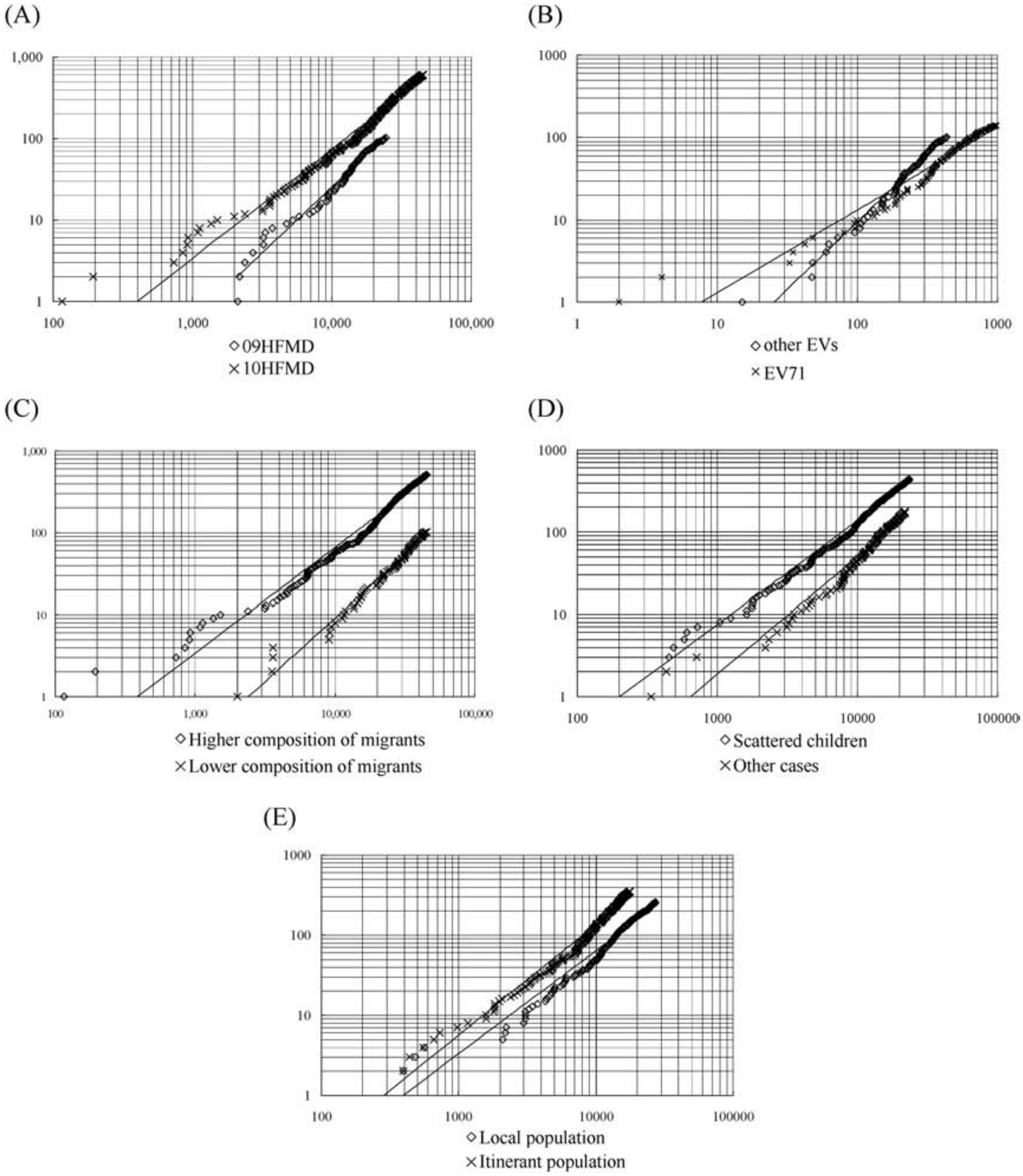

Fig. 1. The log-log plots of cumulative numbers of infected cases and severe cases of HFMD in Beijing. The vertical axis indicates severe cases of HFMD and the horizontal axis the infected cases. (A) The log-log plot of 2009 and 2010. (B) The log-log plot of different pathogens. The k of EV71 was 1 and that of other EVs was 1.636. The severity of infection by other EVs overlapped EV71 when the infection number was <168. (C) The log-log plot of different composition of migrants. (D) The log-log plot of scattered and other cases. (E) The log-log plot of itinerant and local population. All of the lines were drawn and k was >1.

Table 2. Log-log equation of cumulative numbers of infected and severe cases

Classification	Slope	Constant	N_0	Adjusted R^2	F	*P*
2009	1.617	−5.063	1352	0.975	3984.889	<0.01
2010	1.337	−3.479	400	0.972	21260.378	<0.01
EV71	1.007	−0.897	8	0.829	1825.912	<0.01
Other EVs	1.636	−2.296	25	0.981	5203.970	<0.01
Higher composition of migrants	1.289	−3.338	389	0.967	14788.934	<0.01
Lower composition of migrants	1.554	−5.256	2411	0.977	4363.219	<0.01
Scattered children	1.288	−3.395	432	0.965	11957.645	<0.01
Other cases	1.405	−4.35	1248	0.969	5445.748	<0.01
Itinerant populations	1.297	−3.515	513	0.985	22810.335	<0.01
Local populations	1.336	−3.883	806	0.919	2923.538	<0.01

2010 indicated that these viruses can cause severe infection when the number of infectors remains low (Fig. 1B). The coefficient k of the EV71 infection was about 1, and the severity was calculated as 12.5%. The coefficient k was higher for the other EVs (Table 2), and the severity of infection by other EVs would overlap EV71 when the infection number was <168. EV71 and other EVs played an important role in severe cases of HFMD. The increase in HFMD severity in Beijing in 2010 might partially be explained by the higher prevalence of EV71 and other EV infections and their co-infections.

Previous study has found that scattered children and migratory populations had higher infection severity than other populations (6). According to the ratio between residents and non-residents, taking 0.40:1 as the boundary, Beijing was divided into high migrant areas and low migrant areas. All log-log plots (Fig. 1C, D, and E) of cases in both areas and in different populations (scattered children and other children, migrant population or local population) were statistically significant (Table 2) and had $k > 1$. More vulnerable populations should have been involved as the infected population and severity increased. Districts with higher populations of migrants, transient populations, or scattered children had lower N_0. These populations were vulnerable to HFMD and cases were more severe in these populations.

In conclusion, the log-log plot of the cumulative numbers of infected cases and severe cases of HFMD clearly and directly reflected the epidemic progression. Itinerant populations and scattered children were vulnerable populations to HFMD. Lower N_0 indicated pathogenic mutations or pathogenic spectrum changes. The rising severity of HFMD in 2010 in Beijing could be a result of an increased proportion of more aggressive strains. If the plot indicated $k > 1$, emergency pathogenic surveillance and vulnerable population protection measures should be enhanced to reduce the total cases, thus indirectly decreasing the probability of infection as well as the severity, and deceasing incidence in vulnerable populations.

Conflict of interest None to declare.

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