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A New Method for Monitoring and Forecasting the Case-Fatality Rate in Ongoing Epidemics and Its Evaluation Using Published Data of SARS in 2003, H1N1 Pandemic in 2009/2010, Hand-Foot-Mouth Disease in China in 2009/2010, and Cholera in Haiti in 2010

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The log-log plot of the cumulative numbers of infected (X) and deceased (Y) cases over the course of the 2009 H1N1 influenza pandemic gave a straight line which could be expressed by the equation $\log Y = k\log X - k\log N_o$ (1), where N_o is the intercept the X axis, in other words the number of infected cases when the first death occurs (i.e., $Y = 1$). The coefficient k represents the slope of the straight line. The case-fatality rate R can be derived from the above equation as $R = X/Y = (X/N_o)^k/X$, thus meaning that R is a function of X. However, in the case where $k = 1$, R is independent of X and is given by the equation $R = 1/N_o$.

Interestingly, in the case of the 2009 H1N1 influenza pandemic, k was close to 2 in all WHO regions except Mexico, the source of the epidemic, meaning that the case-fatality rate continued to increase over time (1,2). This apparently curious phenomenon can be explained by postulating the existence of two populations: a normal population and a smaller population in which the virus spreads more quickly and has a higher mortality rate (3). It remains to be seen, however, to what extent the above equation is applicable to other epidemics.

Figure 1 shows plots for the hand-foot-mouth disease (HFMD) epidemic in China (May 2008–May 2010) (4), the cholera epidemic in Haiti (October 22–November 3, 2010) (http://new.paho.org/disasters/index.php?option=com_content&task=view&id=1423&Itemid=1), and the 2009 H1N1 influenza pandemic in South-East Asia Reogion (SEARO) (2). The coefficient k was about 1 for both HFMD and cholera (slightly less than 1 for cholera and slightly more than 1 for HFMD), implying that these pathogens spread in a near homogenous population (3). In this case, the case-fatality rate is given simply by the inverse of N_o, which was about 1/10 (10%) for cholera in Haiti and 1/4,000 (0.025%) for HFMD in China. It should be noted that the slope of the HFMD plot remains constant despite the large seasonal variation (highest in April–July, and lowest in January–February) (4). These plots are clearly different from the plot for the 2009 H1N1 Pandemic in SEARO.

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In general, the receiving population is not homogenous in terms of vulnerability to infections, especially elderly people, young children, those with chronic diseases, etc. The question therefore remains as to why k was not >1 for HFMD and cholera. It should be remembered that the two-population model requires that, for k to be >1, the population should contain a sub-population with both higher transmission and mortality rates (3). The reason why k was 1 for cholera and HFMD therefore lies in the fact that both these infections lacked an environment where their pathogens are transmitted more efficiently than in the community (although there may well have been a population more vulnerable to the infection).

Figure 2 shows the same analysis for severe acute respiratory syndrome (SARS) in 2003 (http://www.who.int/csr/sars/archive/en/). Two different patterns are observable, one with $k = 1$ and one with $k = 3$, with China, Canada, and Taiwan belonging to the former and Hong Kong and Singapore to the latter. The plot for the world total is intermediate, with a k value of slightly less than 2.

The case-fatality rate in the former group ($k = 1$) was calculated to be 12.5% (1/8) for Canada and Taiwan and 5% (1/20) for China (N_o was obtained by extrapolating the straight line to the X axis, which was 8 for Canada and Taiwan and 20 for China). As the initial part of the plot for Taiwan was steeper than that for Canada, the epidemics in Canada and Taiwan may have been different to some extent. The lower case-fatality rate in China compared with Taiwan fits well with the observation that the epidemic occurred in the community in China whereas it occurred in a large hospital in Taiwan.

As already mentioned, a situation where $k > 1$ occurs when the receiving population consists of a normal population and smaller population in which the virus spreads more rapidly with higher mortality (3). Such a situation fits well with that encountered in the latter group (Singapore and Hong Kong), in which the SARS outbreak occurred in large hospitals, where the virus can spread faster on account of the confined environment, as well as in the community, where the virus spreads less efficiently (5). The N_o value obtained by extrapolation was 30 for Hong Kong and 70 for Singapore. N_o is expected to be larger when the epidemic in-

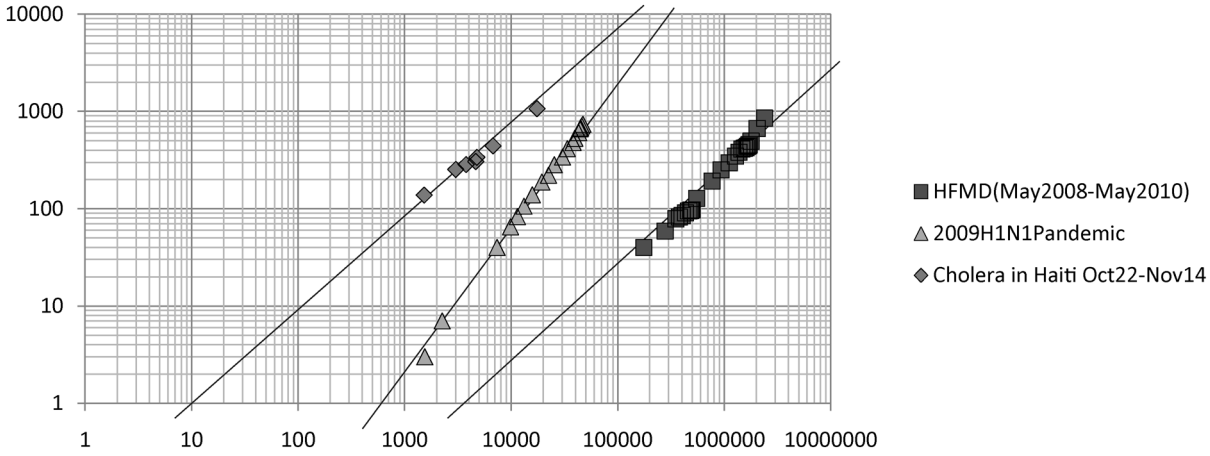

Fig. 1. The log-log plot of the cumulative numbers of infected and deceased cases for cholera in Haiti in 2010 (October 22–November 14), HFMD in China from May 2008 to May 2010, and 2009 H1N1 influenza pandemic in SEARO (2). The vertical axis indicates deceased cases and the horizontal axis the symptomatically infected cases. The lines for HFMD and cholera were drawn so that k = 1.

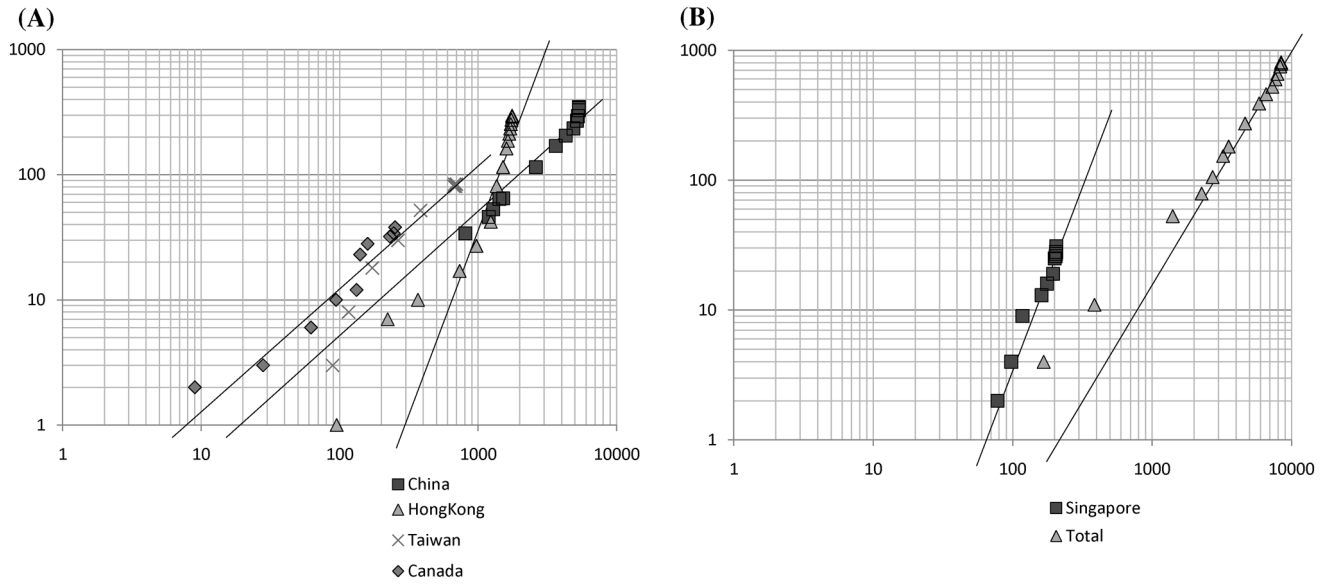

Fig. 2. The log-log plot of the cumulative numbers of infected and deceased cases for SARS in 2003. The plots for China (March 27–July 4), Hong Kong (March 17–July 4), Taiwan (May 1–June 20), and Canada (March 17–July 4) are in Fig. 2A and those for Singapore (March 27–May 30) and the world total (March 17–July 4) in Fig. 2B. The first plot corresponds the day when the first mortal case appeared, and the last plot is the day when the morbidity/mortality stopped increasing. The lines for China, Taiwan, and Canada were drawn so that k = 1. The line for Hong Kong may consist of two parts, the initial part with k about 1 and the later part with k = 3. The vertical axis indicates deceased cases and the horizontal axis the symptomatically infected cases.

volves the more normal population in the community (3), therefore more people from the community must have been involved in Singapore than in Hong Kong.

Although Taiwan was similar to Singapore and Hong Kong in that the SARS outbreak occurred in a hospital, the k value for Taiwan (one) differed notably from those for Singapore and Hong Kong. This is probably due to the fact that the SARS epidemic in Taiwan occurred almost exclusively in a large hospital, thus meaning that the receiving population was quite homogenous (5).

The above observations confirm that the equation obtained using the 2009 H1N1 influenza pandemic (1) can be applied to other epidemics.

The case-fatality rate is expressed as ''the percentage of the number of persons diagnosed as having a specific disease who die as a result of that illness. This term is most frequently applied to a specific outbreak of acute disease *in which all patients have been followed for an adequate period of time to include all attributable deaths*'' (italics added by the author) (6). As stated above, R changes with time in those cases where $k \neq 1$. In other words, the case-fatality rate defined above cannot be obtained till the epidemic is over. However, use of the log-log plot allows us to determine, with a certain degree of confidence, how many patients will die for a given number of patients, even when $k \neq 1$. For the cholera epidemic in Haiti, for example, we can predict that 10,000 people will die if 1% of the whole population (9,648,924 in 2010, http://www.indexmundi.com/

haiti/population.html) is symptomatically infected in the coming months.

The log-log plot of the cumulative numbers of infected and deceased cases during the course of an epidemic will therefore be useful both for monitoring that epidemic and for predicting the expected number of casualties.

Conflict of interest None to declare.

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