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Estimation of Basic Reproduction Number of Enterovirus 71, Coxsackievirus A6 and A16 in Hand, Foot, and Mouth Disease Outbreaks in Singapore

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Objective

To estimate the basic reproduction number of enterovirus 71, coxsackievirus A6 and A16 in hand, foot, and mouth disease outbreaks in Singapore, for a better understanding of the transmission dynamics of these enteroviruses.

Introduction

Hand, foot and mouth disease (HFMD) is a common childhood viral infection, characterised by a brief febrile illness, vesicular rashes on the hands and feet and mouth ulcers. HFMD is endemic in Singapore, with more than 50% of cases occurring in children below 5 years of age.[1] Enterovirus 71 (EV71), coxsackievirus A6 (CA6) and A16 (CA16) were the major enteroviruses causing nationwide HFMD epidemics in Singapore in recent years. We estimated the basic reproduction number (R_0), which measures the infectiousness of a pathogen in a given population, of these enteroviruses to have a better understanding of the transmission dynamics.

Methods

HFMD is a legally notifiable disease in Singapore, and medical practitioners are required to notify all cases of HFMD to the Ministry of Health (MOH). Educational institutions are also required to report to the MOH all outbreaks of HFMD in their institutions. An outbreak is defined as ≥2 cases of HFMD with onset of illness occurring within 10 days in the same institution for investigation and management by the MOH. We merged records of all cases from HFMD outbreaks from 2007 to 2012 with laboratory results from enterovirus surveillance. Outbreaks which occurred in childcare centres and kindergartens with ≥10 children infected were reviewed for selection in this study. We estimated R_0 based on the cumulative number of reported cases in the initial growth phase of each outbreak, using a mathematical model with time expressed in terms of the number of incubation periods.[2] The initial growth phase is defined as the period from onset of symptoms of the first case to the date when the number of newly affected cases had peaked or plateaued.

Results

A total of 33 HFMD outbreaks based on the selection criteria were identified, of which 15 were associated with EV71, 13 with CA16, and 5 with CA6. The median number of infected children in these outbreaks was 16 (interquartile range [IQR], 13 - 18), and the median attack rate was 19.8% (IQR, 13.7% - 23.0%). The median duration of the outbreaks was 16 days (IQR, 12 – 20). Assuming an incubation period of 5 days, the median R_0 of EV71 was 3.5 (IQR, 2.36 – 4.53). The median R_0 was estimated to be lowest for CA16 at 2.42 (IQR, 1.85 – 3.36), and highest for CA6 at 5.04 (IQR, 3.57 – 5.16). Based on sensitivity analyses, R_0 was not significantly associated with the number of infected children (p=0.86), the number of exposed children (p=0.94), and the duration of the outbreaks (p=0.05). On the other hand, R_0 for all the three enteroviruses increased when a longer incubation period was assumed (Fig.).

Conclusions

The median R_0 of the three enteroviruses corresponded to the relative sizes of nationwide HFMD epidemics. Nationwide HFMD epidemics associated with CA16 as the dominant circulating enterovirus were of smaller magnitude. The worst epidemic associated with EV71 in 2008 involved fewer HFMD cases compared with the largest epidemic in 2012 which was associated with CA6. These enterovirus-specific R_0 estimates would be helpful in providing insights into the potential growth of future HFMD epidemics for timely implementation of disease control measures.

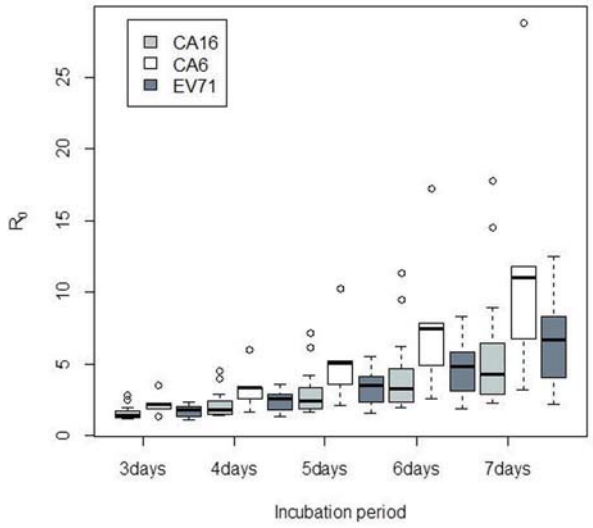

Figure. Estimated R_0 by incubation period and virus type

Keywords

enterovirus; coxsackievirus; reproduction number; hand, foot and mouth disease

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