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SHORT REPORT
Prevalence, seasonality, and peak age of infection of enteric adenoviruses in Japan, 1995–2009

S. K. DEY[1], I. HOQ[2], S. OKITSU[3], S. HAYAKAWA[3] AND H. USHIJIMA[3]*

[1] *Department of Animal and Avian Sciences, University of Maryland, College Park, MD, USA*
[2] *Department of Microbiology, University of Chittagong, Chittagong, Bangladesh*
[3] *Division of Microbiology, Department of Pathology and Microbiology, Nihon University, Japan*

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SUMMARY

A total of 7185 faecal specimens collected from infants and children with gastroenteritis in seven different regions of Japan during 1995–2009 were examined for adenovirus by polymerase chain reaction. Adenovirus was detected in 568 (7·9%) patients. The adenovirus activity peak was in winter and spring seasons (December–March) during the study period in the Japanese paediatric population. During the last 15 years, adenovirus 41 was the most predominant strain in Japan.

Key words: Adenovirus, Japan, prevalence, seasonality.

Human adenoviruses belong to the genus *Mastadenovirus* of the family Adenoviridae and are double-stranded DNA viruses without envelope. Comprehensive controlled studies revealed that the so-called 'non-cultivable' or 'enteric' adenovirus is in contrast to the conventional cultivable 'non-enteric' adenovirus, which is also commonly detected in faecal specimens, and is a frequent primary cause of paediatric gastroenteritis. Adenoviruses are responsible for a wide range of disease symptoms. Enteric adenovirus, however, is also considered to be a significant enteropathogen in association with sporadic cases as well as outbreaks of gastroenteritis in such settings as kindergartens, schools and hospitals [1–3]. Adenoviruses are responsible for a wide range of disease symptoms. To date, more than 51 human adenovirus serotypes have been identified and classified into six subgenera (A–F) based on their biological and genetic characteristics. Of these subgenera, subgenera F represented by two serotypes, i.e. adenovirus types 40 and 41 has been found to be associated with acute gastroenteritis [4, 5]. In Japan, there have been many studies of acute gastroenteritis in children since 1910, even before the discovery of viruses. *Kasei-shoni-kolera* (pseudocholera infantum) or *toki-nyuyoji-gerisho* (infantile winter diarrhoea) are forms of gastroenteritis with symptoms of vomiting, slight fever, dehydration, and whitish, watery stools [6] generally occurring in infants and young children. Seasonality of pathogens can be defined as the appearance of recurrent epidemics at defined periods of the year. Seasonality in disease incidence often reflects associations with weather factors [6]. Climate change is predicted to affect viral infection and may modulate epidemiological outcome, as well as morbidity and mortality of viral infectious diseases. It is predicted that viral infection is attributable to weather fluctuations; therefore climate change may influence the incidence and the spread of the infection [7]. Adenovirus infection may also be influenced by weather fluctuations.

* Author for correspondence: Dr H. Ushijima, M.D., Ph.D., Nihon University School of Medicine, 30-1 Ohyaguchi Kamimachi, Itabashiku, Tokyo 173-8610, Japan.
(Email: ushijima-hiroshi@jcom.home.ne.jp)

Table 1. *Monthly distribution of adenovirus infection in Japan, 1995–2009*

	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May	June
1995	0	0	0	1	7	12	1	2	0	0	0	1
1996	0	1	1	1	—	3	3	5	15	2	0	—
1997	2	0	0	0	4	26	11	20	12	3	3	2
1998	0	0	0	0	2	12	5	3	3	5	2	0
1999	1	3	2	2	12	5	27	16	9	4	8	4
2000	5	2	1	2	3	2	3	3	9	6	4	5
2001	7	1	3	2	2	1	2	0	5	5	2	1
2002	1	1	4	2	1	3	4	3	3	8	3	0
2003	1	1	1	1	5	2	0	2	3	4	5	1
2004	3	0	1	1	11	17	2	7	—	2	4	9
2005	1	1	0	0	2	0	2	2	9	5	6	4
2006	0	1	0	0	0	0	3	5	4	2	7	1
2007	3	0	0	0	5	3	1	4	4	3	8	1
2008	2	1	1	0	4	2	1	2	2	1	1	1
2009	1	1	0	0	1	0	3	0	0	2	1	1

The objectives of this study were to determine the prevalence, seasonality, and peak age of infection of enteric adenoviruses in Japan during 1995–2009.

A total of 7185 faecal specimens were collected from infants and children with acute gastroenteritis in seven different regions from north to the south of Japan (Sapporo, Tokyo, Maizuru, Osaka, Saga, Kagawa, Kurume) during July 1995 to June 2009. In this period, adenovirus analysis was performed systematically on all stool samples by polymerase chain reaction (PCR). Adenovirus was further characterized for genotypes by a sequencing method [8]. We determined the seasonality of adenovirus-associated disease by plotting the percentage of the total number of annual cases that occurred in each month. Monthly distribution of adenovirus was defined after adjusting the epidemic curves according to a 3-month unweighted moving average (mean) [6, 7]. The 'peak' month during the adenovirus season was then defined as that during which the greatest numbers of adenovirus-positive specimens were collected. We analysed the laboratory-confirmed adenovirus cases between 1995 and 2009. We used November as the start month of the adenovirus season for convenience, given that the annual adenovirus season commences between November and May during the study period. To ascertain any shift in the peak, the Mann–Whitney U test was used for analysis of the relationship between duration from August to the peak month (beginning of peak duration) during the 15 seasons. All calculations were performed with SPSS for Windows version 13.0 (SPSS Inc., USA), and significance was set at $P<0{\cdot}05$ [6, 7].

Between 1995 and 2009, a total of 7185 stool samples were received from patients aged <15 years with acute gastroenteritis for microbiological study. Adenovirus was detected in 565 (7·9%) patients. The annual number and percentage of detected patients with adenovirus in 1995–2009 were 10·4% (24/231), 8·1% (31/381), 15·4% (83/537), 6·5% (32/493), 13·5% (88/650), 9·4% (45/477), 6·2% (31/495), 8% (33/413), 6·5% (26/397), 11·9% (57/477), 6·2% (32/513), 5·2% (23/443), 6·2% (32/513), 2·9% (18/607), and 1·8% (10/553), respectively (Table 1). The highest detection rates of adenovirus were in December (15·6%, 88/565) followed by March (13·8%, 78/565), February (13·1%, 74/565) and January (12%, 68/565) and the lowest detection rates were in October (2·1%, 12/565) followed by August (2·3%, 13/565) and September (2·5%, 14/565). Seasonal decrease in adenovirus diarrhoea occurred annually in Japan (Table 1). Peak adenovirus activity occurred between December and March during the study period (1995–2001). A marked finding of this study was that a low number of adenovirus-positive cases occurred in the warm summer months in Japan. Another interesting feature of this study was that the number of adenovirus-positive cases decreased year by year in Japan. During the last 15 years, adenovirus 41 (Ad41) was the most predominant strain in Japan followed by Ad40, Ad5, Ad1, Ad3, and Ad2, respectively.

Epidemiological studies have detected adenoviruses in stool samples collected from infants and young children with acute gastroenteritis, in the developed and developing world [1, 8–10]. A number of research groups in Japan have confirmed that most

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gastroenteritis cases caused by adenovirus occurred during the winter time and were related to ambient temperature. Our analysis, based on laboratory studies during the past 15 years, shows that the adenovirus peak was observed mainly in winter and spring seasons (December–March) in Japan, with statistical significance ($P=0{\cdot}001$), in accord with laboratory data from seven regions (Sapporo, Tokyo, Maizuru, Osaka, Saga, Kagawa, Kurume) of Japan for 1995–2009. The typical pattern of regular adenovirus epidemics that appear during cold months in other countries is similar to that observed in our region in the 1995–2009 period of this study. Seasonality in disease incidence often reflects associations with weather factors [1, 6–8].

Data from previously published studies from 1995 to 2009 have shown that adenovirus is a universal cause of acute gastroenteritis in Japanese infants and children [7–10]. Ad41 was the most predominant strain in Japan. It should be noted that the overall pattern of serotypes was similar to those described in other countries of Asia [1].

In this study we found that adenovirus has been mostly associated with gastroenteritis in infants and children aged <3 years. Over a 15-year period, the present study collected information on diagnosed cases of adenovirus infection and their epidemiological features in a specific geographical area and a well-defined population, i.e. children aged <5 years.

The data from our study demonstrated the cold weather predominance of adenovirus-associated disease in Japan. This finding was independent of the study setting (data not shown), the age of the patients, or the detection methods used and has many implications concerning the route of adenovirus transmission. Winter seasonal transmission is a key epidemiological feature of rotavirus and norovirus, important gastrointestinal pathogens for which airborne transmission has been postulated [7]. Some investigators postulated that the winter peak of viruses may be related to airborne spread [7]. We assumed that winter seasonality of adenovirus-associated disease may also be associated with airborne spread as a secondary route.

In conclusion, the prevalence of adenovirus infection in Japan was significantly high (7·9%). Therefore, adenovirus is considered to be an important enteropathogen responsible for viral gastroenteritis in infants and children in Japan. Although the importance of adenovirus gastroenteritis as a prime cause of morbidity and mortality is well recognized, very few studies have been conducted to evaluate the prevalence and seasonality of adenovirus-related gastroenteritis in infants and children. This paper may provide some important clues to the aetiology of viral gastroenteritis in the Japanese paediatric population.

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DECLARATION OF INTEREST

None.

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