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Full Length Research Paper

Epidemiological and clinical characteristics of gastroenteritis associated with enteric adenovirus in hospitalized children in Bushehr Province, Iran

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Enteric adenoviruses are one of the most significant etiological agents of severe viral gastroenteritis among infants and young children worldwide. This study was conducted to evaluate the clinical and epidemiological features of enteric adenovirus gastroenteritis in hospitalized children less than 7 years of age in Borazjan, Bushehr Province, Iran. From October 2008 to September 2010, stool specimens from 375 children suffering from acute diarrhea were investigated for the presence of enteric adenoviruses using enzyme immunoassays (EIA). Demographic and clinical information were obtained through a standard questionnaire and analyzed by SPSS software. Out of the total collected samples, 5.1% were positive for enteric adenoviruses. Of the adenovirus episodes, 68.42% occurred during the first 2 years of life (*P* = 0.640). The highest prevalence of infection was identified in the spring (63.16%), followed by the autumn (21.05%), winter (10.53%) and summer (5.26%) seasons, respectively (*P* = 0.001). The most common clinical symptoms included diarrhea (84.21%), moderate dehydration (63.16%), fever (57.89%) and vomiting (42.10%). Overall, 69.23% of the children with acute gastroenteritis were not breast-fed and 23.08% were breastfeeding at the time of presentation of the adenovirus infection (*P* = 0.04). This study highlights the importance of enteric adenoviruses as an etiological agent of acute gastroenteritis, particularly among children less than 2 years old and during the cold seasons.

Key words: Enteric adenoviruses, gastroenteritis, epidemiology, Iran.

INTRODUCTION

Despite the success of the current public health services and hygiene control in the water supply and sanitation, diarrhea remains the second leading cause of death in children aged <5 years old worldwide (Black et al., 2010).

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Recent investigations have revealed that diarrhea disease is responsible for 17% of the mortality rate around the world among children less than five years old (Mathers et al., 2009). Several different groups of enteric viruses have been reported to be major etiologic agents of acute infectious diarrhea in the pediatric population. These viruses include rotaviruses, adenoviruses, noroviruses and sapoviruses (Wold and Horwitz, 2007). Of these, group A rotavirus is the most significant cause

of severe diarrhea in infants and young children worldwide (CDC, 2008; Kargar et al., 2011a). Recent studies have indicated adenoviruses to be the second major causative agent of gastroenteritis after rotaviruses (Dey et al., 2009b; Simpore et al., 2009; Ozdemir et al., 2010). Adenovirus infection occurred most commonly within the first 2 years of life (Jarecki et al., 1993; Banyai et al., 2009; Dey et al., 2011). Epidemiological studies in different regions of the world have shown that adenovirus infection occurs throughout the year with increased incidence during the winter and the months of February to March (Jarecki et al., 1993; Modarres et al., 2006; Bányai et al., 2009; Dey et al., 2011). The clinical symptoms of enteric adenovirus infection have been characterized as watery, non-bloody diarrhea with low grade fever, vomiting, abdominal pain and dehydration in children. These symptoms are significantly similar to those observed in patients infected with rotavirus gastroenteritis. (Jarecki et al., 1993; Aminu et al., 2007; Kargar et al., 2011b; Rimoldi et al., 2011). Studies conducted in different regions of the world have indicated that enteric adenoviruses are responsible for 1.35 to 10.4% of the cases of acute gastroenteritis among infants and children <5 years of age (Ospino et al., 2008; Kamel et al., 2009; Simpore et al., 2009; Moyo et al., 2011; Zhang et al., 2011). In Iran, very little data on illness caused by adenovirus has been collected. These studies have revealed that 2.3 to 6.7% of childhood diarrhea hospitalizations are due to adenovirus infection, but epidemiological data is still incomplete (Saderi et al., 2002; Modarres et al., 2006; Hamkar et al., 2010).

The objective of the current study was to assess the clinical and epidemiological features of enteric adenovirus infections in hospitalized children aged <7 years old with acute gastroenteritis in Borazjan, Bushehr Province, Iran.

MATERIALS AND METHODS

Specimen collection

This cross sectional descriptive study was done on stool specimens from children aged <7 years old who were hospitalized with gastroenteric symptoms in 17 Shahrivar Hospital in Borazjan, Bushehr Province, Iran during October 2008 to September 2010. All the fecal specimens were transported to the infectious disease unit laboratory and stored at -70℃ until the time of assay. All samples underwent only one cycle of thawing and freezing prior to characterization. A standard structured questionnaire was used to obtain the information regarding the age, sex, duration of hospital staying, severity of clinical symptoms and type of feeding (as breast/bottle feeding) for each case. According to WHO's recommendation, all the children presented gastroenteritis were classified in specific age groups (for example, 0–2, 3–5, 6–8, 9–11, 12–17, 18–23, 24–35, 36–47 and 48–59 months) so that age-specific incidence rates of hospitalization can be calculated (WHO, 2009).

Adenovirus detection

All fecal specimens were screened for the presence of enteric adenoviruses by using the enzyme immunoassay (EIA) (Adenovirus Antigen, Generic Assays kit, Dahlewitz, Germany), according to the manufacturer's instructions. Briefly, 10% stool suspension was added to the wells containing solid phase immobilized murine monoclonal antibodies. Simultaneously 100 µl of a monoclonal antibody conjugated to horseradish peroxidase (HRP) was added to the wells and incubated for 60 min. After washing, 100 µl of substrate was added and incubated for 10 min at the room temperature. The enzymatic reaction that converts the colourless substrate solution of 3, 3′ 5, 5′-tetramethylbenzidine (TMB) to a blue colour was stopped with H_2SO_4 (0.25 M). The optical density (OD) of the solution was read at 450 nm and specimens having OD values above the cut-off value (0.2 + OD of the negative control) were considered positive for adenovirus antigens.

Data analysis

Data was statistically analyzed by SPSS version 17 (SPSS Inc., Chicago, IL, USA). Chi-square, ANOVA and Fisher's exact tests were used to determine the significance of difference observed between 2 different groups of patients. P values <0.05 were considered statistically significant.

RESULTS

A total of 375 stool samples were collected from hospitalized children less than 7 years of age. All patients had diarrhea for a period of 1 to 5 days before hospitalization. Adenoviruses were detected in 19 of 375 (5.1%) faecal specimens analyzed for the presence of enteric adenovirus antigen by EIA. Adenoviruses were detected more often in males (52.63%) than in females (47.37%). There were no statistically significant differences between sex distribution and adenovirus infection (P = 0.384). All the patients with acute diarrhea were between the ages of 1 and 83 months, and the median age was 22 months (Table 1). The age group analysis revealed that the highest infection rate was among children under 2 years old, counting for 68.42% of all adenovirus-positive cases. Children between 12 to 17 months of age were the most affected (21.05%) (P = 0.640) (Table 1). According to the season distribution, it was observed that adenovirus infection was detected throughout the year but the relative frequency of adenovirus gastroenteritis was highest in the cold seasons of the year. The highest prevalence of infection was identified in the spring (63.16%), followed by the autumn (21.05%), winter (10.53%) and summer (5.26%), respectively. A significant relationship was also found between adenovirus infection and seasonal distribution (P = 0.001). Adenoviruses were detected continuously in a 5-month period lasting from February to June. Adenoviruses were detected most frequently in April to May (P = 0.002) (Table 2). The observed clinical features

Table 1. Distribution of age groups in patients with enteric adenoviruses from October 2008 to September 2010.

Age groups (Month)	Adenovirus group (n = 19) (%)	Non-adenovirus group (n = 356) (%)	Global No. = 375 (%)
0-2	-	6 (1.68)	6 (1.6)
3-5	-	39 (10.95)	39 (10.4)
6-8	3 (15.79)	42 (11.8)	45 (12.0)
9-11	3 (15.79)	45 (12.64)	48 (12.8)
12-17	4 (21.05)	85 (23.88)	89 (23.73)
18-23	3 (15.79)	37 (10.39)	40 (10.67)
24-35	2 (10.53)	32 (8.99)	34 (9.07)
36-47	-	29 (8.15)	29 (7.73)
48-60	2 (10.53)	14 (3.93)	16 (4.27)
61-83	2 (10.53)	27 (7.58)	29 (7.73)

Data within each group is expressed as number of patients (%).

Table 2. Monthly distribution of enteric adenoviruses from October 2008 to September 2010.

Months	No. of patients	No. of adenovirus positive	Rate (%)
Jan	18	-	-
Feb	24	1	5.26
Mar	3	1	5.26
Apr	11	4	21.05
May	56	6	31.58
Jun	28	2	10.53
Jul	9	-	-
Aug	8	1	5.26
Sep	5	-	-
Oct	14	-	-
Nov	126	2	10.53
Dec	73	2	10.53
Total	375	19	100

in children with acute diarrhea and the type of feeding used are shown in Table 3. The survey of clinical manifestations revealed that diarrhea (84.21%), moderate dehydration (63.16%), fever (57.89%) and vomiting (42.10%) were the most common symptoms in children with adenovirus gastroenteritis. The frequency of the enteric adenovirus gastroenteritis among infants less than 24 months of age who were breast-fed, bottle-fed and using both of nutrition status at the time of presentation of infection was 23.08%, 69.23% and 7.69%, respectively (P = 0.04).

DISCUSSION

Enteric adenoviruses are one of the most common pathogens associated with acute gastroenteritis in infants and young children not only in the developing countries like Thailand (Herrmann et al., 1988), Tunisia (Sdiri-Loulizi et al., 2009) and India (Dey et al., 2011), but also in industrialized countries like Germany (Oh et al., 2003), Japan (Dey et al., 2009b) and Italy (Rimoldi et al., 2011). In this study, laboratory diagnosis was performed by using the enzyme immunoassays (EIA) technique for antigen detection. From 2008 to 2010, epidemiological study of adenovirus diarrhea in Borazjan, Bushehr Province, Iran, showed a prevalence rate of 5.1% in children less than seven years of age with acute gastroenteritis. This result is comparable to the disease burden of adenovirus reported in other investigates in Iran and different countries which was shown to be responsible for 1.35 to 10.4% of all cases of gastroenteritis (Jarecki et al., 1993; Modarres et al., 2006; Ospino et al., 2008; Kamel et al., 2009; Hamkar et al., 2010; Moyo et al., 2011; Zhang et al., 2011). We detected a relatively high rate of enteric adenovirus

Table 3. Distribution of clinical characteristics and pattern of nutrition in patients with enteric adenoviruses.

Variable	Adenovirus group (n = 19) (%)	Non-adenovirus group (n = 356) (%)	Global No. = 375 (%)	P value
Clinical symptoms				
Diarrhea	16 (84.21)	298 (83.71)	314 (83.73)	0.626
Vomiting	8 (42.10)	172 (48.31)	180 (48.0)	0.387
Fever	11 (57.89)	168 (47.19)	179 (47.73)	0.250
Convulsion	1 (5.26)	9 (2.53)	10 (2.66)	0.543
Abdominal pain	6 (31.58)	119 (33.43)	125 (33.33)	0.409
Dehydration severity				
Severe dehydration	4 (21.05)	58 (16.29)	62 (16.53)	0.119
Moderate dehydration	12 (63.16)	187 (52.53)	199 (53.07)	0.639
Mild dehydration	3 (15.79)	111(31.18)	114 (30.4)	0.387
Nutrition status (infants aged <24months)	**Adenovirus group (n = 13) (%)**	**Non-adenovirus group (n = 255)**	**Global No. = 268 (%)**	
Breast-fed	3 (23.08)	68 (26.67)	71 (26.49)	
Bottle-fed	9 (69.23)	180 (70.59)	189 (70.52)	0.04
Breast-fed and Bottle-fed	1 (7.69)	7 (2.74)	8 (2.99)	

Data within each group is expressed as number of patients (%).

among infants and young children less than 2 years of age, which is in agreement with previous reports in Thailand (Herrmann et al., 1988), Iran (Modarres et al., 2006), Bangladesh (Dey et al., 2009a), Turkey (Ozdemir et al., 2010) and India (Dey et al., 2011). This result highlights that children aged <2 years old are at greatest risk for developing severe diarrhea from an adenovirus infection. Epidemiological studies around the world have revealed that adenovirus diarrhea occurs throughout the year with increased incidence during the cool seasons of year (Jarecki et al., 1993; Modarres et al., 2006; Dey et al., 2009a). Our study demonstrated that there was a significant correlation between the seasonal distribution and adenovirus detection. Adenovirus gastroenteritis occurred throughout the year, with more cases occurring in the spring and winter with a seasonal peak observed in the months of April to May. These findings are in keeping with studies conducted in other countries (Dey et al., 2009b; Hamkar et al., 2010; Ozdemir et al., 2010; Dey et al., 2011). The most common clinical symptom observed in our study was diarrhea, followed by moderate dehydration, fever and vomiting. These findings are similar to those results reported in Bangladesh (Jarecki et al., 1993; Dey et al., 2009a), Nigeria (Aminu et al., 2007), Iran (Modarres et al., 2006; Hamkar et al., 2010) and Italy (Rimoldi et al., 2011). In this study, evaluation of the breastfeeding status of infants aged <24 months of age with acute diarrhea revealed that adenovirus-positive cases were significantly lower among those being breastfed at the time of acute gastroenteritis. This result suggests breastfeeding may be a protective factor against adenovirus infection by moving passive immunity from the mothers to infants. This result was similar to those previously described in other studies (Modarres et al., 2006). On the other hand, the lower frequency of adenovirus infection among those that both breastfed and bottle-fed may be explained with the synergy of these two types of nutrition in reducing the amount of adenovirus disease. But additional studies may be required to elucidate this phenomenon. One limitation of the present study is that true enteric adenoviruses prevalence can be higher than estimated here (5.1%), because in this study only hospitalized children with acute diarrhea have been evaluated and the proportion of adenoviruses infections among children with only home care or outpatient visits have not been estimated. In conclusion, this study provides information on the epidemiology and the prevalence of adenovirus gastroenteritis in children with acute diarrhea in Borazjan, Bushehr Province, Iran. Our results highlight the importance of enteric adenovirus gastroenteritis as one of the important health problems, particularly among children less than 2 years old and during the cold seasons in the population under surveillance.

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