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OUTBREAKS OF HUMAN-HERPES VIRUS 6 (HHV-6) INFECTION IN DAY-CARE CENTERS IN BELÉM, PARÁ, BRAZIL

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SUMMARY

A total of 730 children aged less than 7 years, attending 8 day-care centers (DCCs) in Belém, Brazil were followed-up from January to December 1997 to investigate the occurrence of human-herpes virus 6 (HHV-6) infection in these institutional settings. Between October and December 1997 there have been outbreaks of a febrile- and -exanthematous disease, affecting at least 15-20% of children in each of the DCCs. Both serum- and- plasma samples were obtained from 401 (55%) of the 730 participating children for the detection of HHV-6 antibodies by enzyme-linked immunosorbent assay (ELISA), and viral DNA amplification through the nested-PCR. Recent HHV-6 infection was diagnosed in 63.8% (256/401) of them, as defined by the presence of both IgM and IgG-specific antibodies (IgM+/IgG+); of these, 114 (44.5%) were symptomatic and 142 (55.5%) had no symptoms ($p = 0.03$). A subgroup of 123 (30.7%) children were found to be IgM-/IgG+, whereas the remaining 22 (5.5%) children had neither IgM nor IgG HHV-6-antibodies (IgM-/IgG-). Of the 118 children reacting strongly IgM-positive (≥ 30 PANBIO units), 26 (22.0%) were found to harbour the HHV-6 DNA, as demonstrated by nested-PCR. Taken the ELISA-IgM- and- nested PCR-positive results together, HHV-6 infection was shown to have occurred in 5 of the 8 DCCs under follow-up. Serological evidence of recent infections by Epstein-Barr virus (EBV) and parvovirus B19 were identified in 2.0% (8/401) and 1.5% (6/401) of the children, respectively. Our data provide strong evidence that HHV-6 is a common cause of outbreaks of febrile/exanthematous diseases among children attending DCCs in the Belém area.

KEYWORDS: Herpesvirus type 6; Outbreaks; Day-care centers.

INTRODUCTION

The human herpesvirus type-6 (HHV-6) was first isolated in 1986, by SALAHUDDIN *et al*.[45], from lymphocytes of patients with lymphoproliferative disorders or acquired immunodeficiency syndrome. Although *in vivo* viral replication occurs mainly in $CD4^+$ T-lymphocytes[19,36], a number of other cell lines were shown to be susceptible to HHV-6 infection[35,40]. In addition, HHV-6 may induce clear cytopathogenic effect when infecting lymphocyte cultures *in vitro*[40,50].

Seroepidemiological studies conducted in several countries throughout the world provided evidence that HHV-6 infection occurs both in infants and adults, as suggested by prevalence rates of antibodies that vary from 45% to 63% and 52% to 97%, respectively[1,6,24,37,42,46]. An additional finding from serosurvey studies is that infants become infected very early in life, in general before the age of 3 years[6,37,53]. Two HHV-6 variants (A and B) have been identified to date. While HHV-6B variant accounts mostly for cases of exanthem subitum (ES) and other less common clinical presentations among infants[13,42,43], a role has not yet been firmly established for HHV-6A as a human pathogen[47]. In Japan, 60% of children who have HHV-6 primary infection develop typical ES[30]. In contrast, about 70% of primoinfections among infants in the USA and Europe are characterized by a mild febrile illness that courses with or without exanthem[42,43]. A variety of other clinical conditions have also been associated with HHV-6 infections namely mononucleosis-like syndrome, sarcoidosis, hepatitis and febrile convulsion[1,5,14,25,27,28,34].

The first studies dealing with HHV-6 infection in Brazil were carried out by LINHARES *et al.*[33], who recorded seroprevalence rates of 76.5% and 77.2% in Brazilian and Japanese immigrants, respectively, in the north-eastern region. Subsequent serosurvey studies conducted in the Amazon region of Brazil yielded prevalence rates of HHV-6 antibody that ranged from 5.4% to 14.9%, among amerindians[16], and from 75% to 100% in the urban communities[17]. Furthermore, the occurrence of ES in Brazil in association with HHV-6 infection was first reported on both clinical and laboratorial grounds, by FREITAS *et al*[18].

Worldwide, there have been few reports on outbreaks caused by HHV-6. Both serological and clinical data indicate that extensive outbreaks (mostly of ES) occurred in hospitals, London, UK[23], and in

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an orphanage, Osaka, Japan[39], with incidence rates of HHV-6 infection ranging from 20% to 100%. These were explosive epidemics that occurred during the summer months, affecting both children and adults, and the emergence of cases followed in general a short incubation period. In Brazil, outbreaks due to HHV-6 infection have not so far been reported.

The present report describes the occurrence of outbreaks associated with HHV-6 infection affecting children who attended several day-care centers in the urban area of Belém, Brazil.

MATERIALS AND METHODS

The present surveillance was conducted between January and December 1997 and involved 8 community DCCs which were located in 4 neighborhoods (*Cremação*, *Guamá*, *Jurunas* and *Terra-Firme*) of Belém, northern Brazil. Six of these DCCs (*Alcindo Cacela*, *Caraparu*, *Monte Alegre*, *Santa Rosa*, *São Domingos* and *São Silvestre*) belonged to the municipality's official primary school system, whereas 2 of them (*Boa Esperança* and *Orquídea*) were settled through the neighborhoods' community leadership. DCCs included in general 1-4 rooms for 30-40 children each. These children stay at the DCCs for about 11 hours (7 am to 6 pm) per day, from Monday to Friday. Apart from primary teaching, playroom activities and feeding are planned. Families seeking for these day-care facilities are mostly from the low socioeconomic level.

Overall, 730 children of both sexes were attending the 8 DCCs when the present surveillance was carried out. Each DCC housed between 40 and 130 children whose ages ranged from 1 to 7 years (mean age, 3.5 years).

From January to December 1997 regular weekly visits were made to each DCC by a trained field-worker from our staff, primarily to assess the occurrence of outbreaks of febrile/exanthematous disease in these institutional settings. Between October and December 1997 outbreaks of fever (either with or without exanthem) were recorded in all DCCs, lasting an average of 10-15 days and affecting at least 20% of the whole number of children lodged in each of them. During this period, 401 blood samples (one per child) were obtained through antecubital venepuncture, corresponding to approximately 50% of all children per DCC. Sera were kept frozen at –20 °C until being tested for the presence of both IgM and IgG antibodies to HHV-6 using a commercial enzyme-linked immunosorbent assay (ELISA) developed by PANBIO™ (East Brisbane, Australia). This is an assay that includes a solid-phase multi-wells system coated with HHV-6-infected cells, as previously described[4,11,41]. For the determination of HHV-6 immunoglobulin M (IgM) sera were tested at single 1:100 (v/v) dilutions, with previous removal of IgG. This eliminates interference by HHV-6 IgG and IgM rheumatoid factor. All serum samples yielding optical density (OD) values of greater than twice of the mean absorbance of the "cut off" were regarded as suggestive of recent HHV-6 infection; this corresponds to > 20 IgM PANBIO units. An aliquot of the plasma samples was used for separation of peripheral blood mononuclear cells (PBMCs) by centrifugation through Ficoll-Hypaque gradient (Pharmacia™, Uppsala, Sweden), as described before[50]. The detection of HHV-6 DNA was performed by polymerase chain reaction (PCR) in both the whole plasma sample and PBMCs which were kept frozen (-70 °C) until being assayed. Only IgM-positive serum samples yielding ≥ 30 PANBIO units (n = 118) were subjected to PCR assay. This was performed in two steps, essentially as reported before[26,48,49]. First amplification was carried out using a mixture of external oligonucleotide primers designated as *EX1* and *EX2*, followed by a second amplification (the nested PCR) including a mixture of internal primers *IN3* and *IN4*.

Conventional ELISA was used for the detection of both IgM and IgG to measles, rubella, parvovirus B19, Epstein-Barr virus and cytomegalovirus, as previously reported[2,9,12,31,44]. Samples were also tested by haemagglutination-inhibition (HI) assay[22] for the determination of antibodies to Mayaro, Oropouche and dengue viruses, which are well-known viral agents of exanthematous illnesses in the Amazon region. In addition, a immunofluorescence indirect assay (Kit Chemicon™ International, Temecula, CA, USA) was used for diagnosis of respiratory viruses in a subgroup of 40 symptomatic children such as adenovirus, influenza, parainfluenza and respiratory syncitial virus.

The present survey covered a representative sample of the population and data were analyzed using the EPI INFO software, version 6.0 (Atlanta, GA, USA). Rates were compared by using the Mantel-Haenszel chi square test of association or Fisher's exact test, as appropriate. Significance was defined as $p < 0.05$.

RESULTS

Overall, 730 children were enrolled to participate in this follow-up study. Both serum- and- plasma samples were obtained from 401 (55.0%) of them and tested for the presence of HHV-6 antibodies. Table 1 shows that: (i) an IgM+/IgG+ seroresponse was noted in 256 (63.8%) of the children; (ii) previous HHV-6 infection was identified in 123 (30.7%) children who reacted IgM-/IgG+; and (iii) 22 had neither IgG nor IgM antibodies to HHV-6 (IgM-/IgG-). The distribution of IgM seropositivity, according to the DCC and sex, is demonstrated in Table 2. The prevalence rates ranged from 54.3% (DCC *Orquídea*) to 76.0% (*Caraparu*). Serological evidence of recent infection by HHV-6 occurred in 68.6% and 59.4% of female and male children, respectively. In the former group, IgM-seropositivity rates ranged from 65.5% to 71.4% for 4-5 and <3 year-old groups, respectively; in the latter one, range was of 50.0% to 68.0% for the <3 and 3-4 year-old groups, respectively.

The results of the nested-PCR are gathered in Table 3 and in Figure 1. The viral DNA was detected in 26 (22.0%) out of the 118 children selected for testing, that is, those yielding HHV-6-IgM positivity values of ≥ 30 PANBIO units. Among these nested- PCR-positive children, 15 were male. Figure 1 illustrates the nested-PCR amplified products obtained from PBMCs of children attending 5 (63.3%) of the 8 DCCs under investigation. Nested-PCR results were similar when testing both plasma and PBMC samples.

The clinical status of the 256 children with serological evidence of current/recent HHV-6 infection (HHV-6 IgM PANBIO units of greater than 20) is specified in Table 4. There were 114 (44.5%) and 142 (55.5%) symptomatic and asymptomatic infections, respectively ($p = 0.03$). The most frequent presentation (89 children, 34.8%) included fever (≥ 39.0 °C) and respiratory symptoms (productive cough and running nose). Less frequently, the following clinical pictures could be recorded, as follows: high fever only that lasted 3-4 days, 17 children (6.6%); maculo-papular exanthematous illness (MPEI), 6 (2.2%); fever and MPEI, 1 (0.4%); and fever, convulsions and watery diarrhoea, 1 (0.4%).

Table 1
Detection of antibodies to HHV-6 in children of eight DCCs*, according to sex. Belém, Pará, Brazil

Neighborhood/ DCC	Month of epidemics (1997)	Sex	Total of children	Total of children with serum samples (%)	Serological status		
					(IgM+/IgG+)	(IgM-/IgG+)	(IgM-/IgG-)
Cremação							
Alcindo Cacela	October	Female	57	33 (58.0)	22 (66.7)	9 (27.2)	1 (3.0)
		Male	43	25 (58.1)	11 (42.3)	10 (40.0)	4 (16.0)
Guamá							
Caraparu	November	Female	18	11 (61.1)	9 (81.8)	1 (9.1)	1 (9.1)
		Male	22	14 (63.6)	10 (71.4)	4 (28.6)	0 (0)
Santa Rosa	November	Female	51	32 (62.7)	24 (75.0)	8 (25.0)	0 (0)
		Male	49	31 (63.3)	19 (61.3)	10 (32.3)	2 (6.4)
Jurunas							
Monte Alegre	December	Female	69	37 (53.6)	27 (72.9)	7 (18.9)	3 (8.1)
		Male	61	33 (54.1)	22 (66.7)	11 (33.3)	0 (0)
São Silvestre	December	Female	52	29 (55.8)	16 (55.2)	9 (31.0)	4 (13.8)
		Male	78	43 (55.1)	26 (60.5)	16 (37.2)	1 (2.3)
Terra Firme							
Boa Esperança	October	Female	37	18 (49.0)	11 (61.1)	6 (33.3)	1 (5.5)
		Male	43	21 (49.0)	13 (61.9)	8 (38.1)	0 (0)
Orquídea	October	Female	36	18 (50.0)	11 (61.1)	6 (33.3)	1 (5.6)
		Male	34	17 (50.0)	8 (47.1)	9 (52.9)	0 (0)
São Domingos	November	Female	41	19 (46.3)	13 (68.4)	5 (26.3)	1 (5.3)
		Male	39	20 (51.3)	14 (70.0)	4 (20.0)	2 (10.0)
Subtotal		Female	361	197 (54.6)	133 (68.6)	53 (26.9)	11 (5.6)
		Male	369	204 (55.3)	123 (60.2)	70 (34.3)	11 (5.4)
Total			730	401 (55.0)	256 (63.8)	123 (30.7)	22 (5.5)

* Day-care centers

Table 2
Distribution of recent HHV-6 infections* according to sex and age in children of eight DCCs** located in the urban area of Belém, Pará, Brazil

Sex/age	Positive/No. tested (%) for **neighborhoods** and DCCs								Total
	Cremação	**Guamá**		**Jurunas**		**Terra Firme**			
(years)	Alcindo Cacela	Caraparu	Santa Rosa	Monte Alegre	São Silvestre	Boa Esperança	Orquídea	São Domingos	
Female									
<3	17/21 (80.9)	0/0 (0)	3/3 (100.0)	4/6 (66.7)	0/4 (0)	2/3 (66.7)	2/3 (66.7)	2/2 (100.0)	30/42 (71.4)
3-4	1/3 (33.3)	3/3 (100.0)	4/5 (80.0)	9/13 (69.2)	3/5 (60.0)	0/3 (0)	4/4 (100.0)	5/5 (100.0)	29/41 (70.7)
4-5	1/3 (33.3)	3/4 (75.0)	4/6 (66.7)	9/11 (81.8)	10/17 (58.8)	5/5 (100.0)	1/4 (25.0)	3/5 (60.0)	36/55 (65.5)
>5	3/5 (60.0)	3/4 (75.0)	13/18 (72.2)	5/6 (83.3)	3/3 (100.0)	4/6 (66.7)	4/7 (57.1)	3/7 (42.9)	38/56 (67.9)
Subtotal	22/32 (68.8)	9/11 (81.8)	24/32 (75.0)	27/36 (75.0)	16/29 (55.2)	11/17 (64.7)	10/18 (55.6)	13/19 (68.4)	133/194 (68.6)
Male									
<3	7/17 (41.2)	0/0 (0)	2/3 (66.7)	2/2 (100.0)	6/12 (50.0)	1/3 (33.3)	0/0 (0)	3/5 (60.0)	21/42 (50.0)
3-4	3/6 (50.0)	2/2 (100.0)	8/9 (88.9)	5/10 (50.0)	6/7 (85.7)	4/6 (66.7)	2/4 (50.0)	4/6 (66.7)	34/50 (68.0)
4-5	0/1 (0)	5/9 (55.6)	3/10 (30.0)	10/16 (62.5)	10/14 (71.4)	1/5 (20.0)	5/10 (50.0)	5/5 (100.0)	39/70 (55.7)
>5	1/2 (50.0)	3/3 (100.0)	6/9 (66.7)	4/6 (66.7)	5/10 (50.0)	7/8 (87.5)	1/3 (33.3)	2/4 (50.0)	29/45 (64.4)
Subtotal	11/26 (42.3)	10/14 (71.4)	19/31 (61.3)	22/34 (64.7)	26/43 (60.5)	13/22 (59.1)	8/17 (47.1)	14/20 (70.0)	123/207 (59.4)
Total	33/58 (56.9)	19/25 (76.0)	43/63 (68.3)	49/70 (70.0)	42/72 (58.3)	24/39 (61.5)	19/35 (54.3)	27/39 (69.2)	256/401 (63.8)

* IgM detection (>20 PANBIO units); **Day-carecenters

Table 3
Detection of HHV-6 DNA in cases of recent infection* in a subgroup (n=118) of children attending eight DCCs**, according to sex. Belém, Pará, Brazil

Neighborhood/DCC	Sex	Total of children with plasma samples/lymphocytes tested (%)	Nested-PCR-results (%) (DNA+)	(DNA-)
Cremação				
Alcindo Cacela	Female	7 (5.9)	0/7 (0)	7/7 (100.0)
	Male	6 (5.1)	1/6 (16.7)	5/6 (83.3)
Guamá				
Caraparu	Female	5 (4.2)	1/5 (20.0)	4/5 (80.0)
	Male	1 (0.8)	0/1 (0)	1/1 (100.0)
Santa Rosa	Female	11 (9.3)	0/1 (0)	11/11 (100.0)
	Male	8 (6.8)	1/8 (12.5)	7/8 (87.5)
Jurunas				
Monte Alegre	Female	15 (12.7)	7/15 (46.7)	8/15 (53.3)
	Male	7 (5.9)	5/7 (71.4)	2/7 (28.6)
São Silvestre	Female	11 (9.3)	3/11 (27.3)	8/11 (72.7)
	Male	20 (16.9)	8/20 (40.0)	12/20 (60.0)
Terra Firme				
Boa Esperança	Female	2 (1.7)	0/2 (0)	2/2 (100.0)
	Male	4 (3.4)	0/4 (0)	4/4 (100.0)
Orquídea	Female	7 (5.9)	0/7 (0)	7/7 (100.0)
	Male	3 (2.5)	0/3 (0)	3/3 (100.0)
São Domingos	Female	7 (5.9)	0/7 (0)	7/7 (100.0)
	Male	4 (3.4)	0/4 (0)	4/4 (100.0)
Subtotal	Female	65 (55.1)	11/65 (16.9)	54/65 (83.1)
	Male	53 (44.9)	15/53 (28.3)	38/53 (71.7)
Total		118 (100.0)	26/118 (22.0)	92/118 (78.0)

* IgM detection (≥ 30 PANBIO units); **Day-care centers

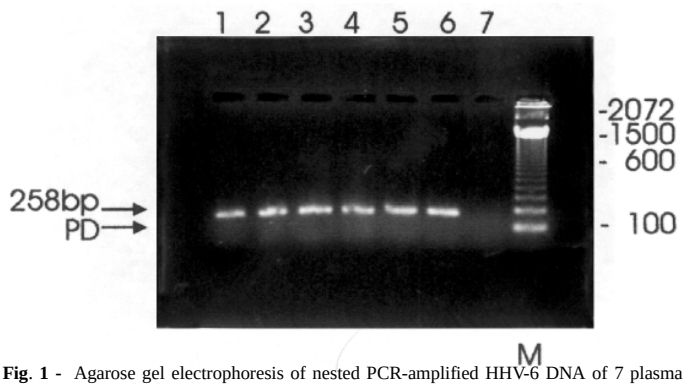

Fig. 1 - Agarose gel electrophoresis of nested PCR-amplified HHV-6 DNA of 7 plasma samples/lymphocytes, stained with ethidium bromide and photographed under U.V light. Lanes 1-5, HHV-6-positive specimens (DCCs: A. Cacela (1), Caraparu (2), S. Rosa (3), M. Alegre (4), S. Silvestre (5); lane 6, positive control; lane 7, negative control ; M denotes molecular-weight; PD denotes primer dimer.

Eight (2.0%) of the 401 children whose sera were taken reacted IgM/IgG-positive for EBV, whereas 6 (1.5%) developed parvovirus B-19 infection. These 14 children had no recent/current HHV-6 infection. No positive results indicative of recent infection were obtained from testing of sera against other pathogens that might be involved in the aetiology of the febrile and/or exanthematous illnesses. There have been no cases of current/recent dengue infection, even though an extensive outbreak was occurring in Belém.

DISCUSSION

Outbreaks of HHV-6 infection sometimes are observed among infants living in institutions, such as hospitals and orphanages, since the transmission is enhanced as a result of close contact between these institutional inmates[23,39]. An environment similar to these settings was noted in the present investigation – the DCCs -, where children were kept in close contact during 10-12 hours per day, therefore making outbreaks more likely to occur.

Table 4
Clinical presentations associated with HHV-6 infection* in children of eight DCCs.** Belém, Pará, Brazil

Neighborhood/DCC	Symptoms (%)					Asymptomatic	Total
	Fever***	Fever + ARI****	Exanthem	Fever+ exanthem	Fever+convulsion+ diarrhoea		
Cremação							
Alcindo Cacela	2 (0.8)	11 (4.3)	3 (1.1)	1 (0.4)	1 (0.4)	18 (7.0)	36 (14.1)
Guamá							
Caraparu	1 (0.4)	4 (1.6)	0 (0)	0 (0)	0 (0)	15 (5.8)	20 (7.8)
Santa Rosa	4 (1.6)	17 (6.6)	3 (1.1)	0 (0)	0 (0)	14 (5.5)	38 (14.8)
Jurunas							
Monte Alegre	0 (0)	20 (7.8)	0 (0)	0 (0)	0 (0)	32 (12.5)	52 (20.3)
São Silvestre	0 (0)	15 (5.8)	0 (0)	0 (0)	0 (0)	13 (5.1)	28 (11.0)
Terra Firme							
Boa Esperança	2 (0.8)	4 (1.6)	0 (0)	0 (0)	0 (0)	22 (8.6)	28 (11.0)
Orquídea	5 (1.9)	4 (1.6)	0 (0)	0 (0)	0 (0)	14 (5.5)	23 (9.0)
São Domingos	3 (1.1)	14 (5.5)	0 (0)	0 (0)	0 (0)	14 (5.5)	31 (12.1)
Total	17 (6.6)	89 (34.8)	6 (2.2)	1 (0.4)	1 (0.4)	142 (55.5)	256 (100.0)

* IgM detection (> 20 PANBIO units); ** Day-care centers; *** > 39 ºC; ****Acute respiratory infection.

Previous studies carried out in temperate countries (eg. England and Japan) have shown the seasonality of epidemics of HHV-6 infection, usually occurring during the summer months[23,39]. The fact that the presently described outbreaks have clustered during October-December, suggests a possible seasonal pattern of HHV-6 infection in our region.

The explosive nature of the outbreaks in DCCs in Belém, together with a significant proportion of children reacting HHV-6 IgM-positive, indicates the high degree of susceptibility among these institutional inmates to a highly transmissible viral agent[23,39].

The gender distribution of seropositivity rates shows no significant differences, as already demonstrated in previous serosurveys conducted in the same setting[17]. Moreover, the predominance of recent infection by HHV-6 in the lowest age-groups (< 3 and 3 to 4 years) sustains previous seroepidemiological data indicating that HHV-6 infections is largely more frequent before 3 years of life[3,7,53,54]. In the present study it is most likely that transmission of HHV-6 had occurred by respiratory droplet infection, resulting in a high number of cases during a short time-interval. This mode of transmission has been supported by several investigations recording the detection of HHV-6 DNA in both saliva and salivary glands[10,15,20,21,29,32].

In our study HHV-6 infection was significantly more likely to be asymptomatic ($p = 0.03$), suggesting that exanthem subitum may not be the predominant outcome of early, primary infection in Belém. It is of interest in this regard to mention the seroepidemiological data from TAKAHASHI *et al*.[51] suggesting that a significant proportion of children may develop HHV-6 symptomless (primary) infection later in life, therefore without having had exanthem subitum (ES).

The detection of specific-IgM in plasma samples from several children, together with the fact that HHV-6 DNA was detected in both plasma and lymphocytes of 26 individuals, suggests that primary infection was largely occurring during the outbreaks in the DCCs in Belém. It should be pointed out that the detection of viral DNA in serum/plasma samples represents a surrogate marker for HHV-6 active infection, mostly in cases of ES[49]. The detection of HHV-6 DNA in 5 of the 8 DCCs in Belém represents an additional evidence that HHV-6 has widely circulated among infants and children (both sexes and several age-groups) during the presently reported outbreaks. It is likely that the nested-PCR-negative results yielded in 92 patients reflect a late sample collection in the course of infection.

Of particular interest in the present survey was the occurrence of a variety of clinical conditions not resembling those related to the typical ES. This is in accordance with previous findings in USA where only 9% of patients with HHV-6 primary infection developed the typical ES[43]. Atypical clinical presentations have been identified in several patients, as follows: (i) exanthem without fever; (ii) acute respiratory symptoms (sore throat, productive cough and running nose) in the absence of cutaneous rash; (iii) watery diarrhoea; and (iv) febrile convulsion. Such unusual clinical presentations of HHV-6 infection early in life have also been identified in previous similar studies[34,43]. It should be pointed out that all illnesses in the present study coursed without any prominent complication or sequelae, as usually observed elsewhere[37,52,53,54]. The limited number of children presenting with convulsion may reflect the low neurotropic potential of the infecting HHV-6 strain[8].

With the exception of 14 (3.5%) children reacting IgM-positive for Epstein-Barr virus (EBV) (n = 8) and parvovirus B19 (n = 6), negative results were yielded when testing sera for antibodies to a variety of other pathogens that might be related to febrile/exanthematous disease in our region. Of note, the possible role of adenoviruses, influenza, parainfluenza and respiratory syncytial virus in the aetiology of respiratory illnesses was also ruled out.

Local studies are currently being planned to assess the genotypic diversity of HHV-6 strains, in view of the apparently broad clinical spectrum of the disease in our region.

RESUMO

Surtos epidêmicos associados à infecção pelo herpesvírus tipo 6 (HHV-6) em creches comunitárias de Belém, Pará, Brasil

Um total de 730 crianças com menos de 7 anos de idade, matriculadas em oito creches comunitárias (CCS) em Belém, Brasil foi acompanhado de janeiro a dezembro de 1997, com objetivo de se investigar a ocorrência de epidemias de infecção pelo HHV-6. Entre os meses de outubro e dezembro de 1997 foram registrados surtos de doença febril–exantemática acometendo cerca de 15-20% da população de cada CC. Amostras de soro e plasma foram obtidas de 401 (55,0%) das 730 crianças participantes, tendo como finalidade a detecção de anticorpos para o HHV-6 e amplificação do DNA viral, utilizando-se o método imunoenzimático (ELISA) e as provas de biologia molecular: reação em cadeia da polimerase (PCR) *nested* PCR. Infecção recente para o HHV-6 foi diagnosticada em 63,8% (256/401) das crianças, as quais, apresentaram anticorpos IgM e IgG (IgM+/IgG+). Dessas, 114 (44,5%) foram sintomáticas e 142 (55,5%) assintomáticas (p=0,03). Um subgrupo de 123 (30,7%) menores foi identificado como previamente imune (IgM-/IgG+) e 22 (5,5%) crianças não apresentaram anticorpos IgM e IgG (IgM-/IgG-). O DNA do HHV-6 foi detectado em 26 (22,0%) das 118 crianças selecionadas, apresentando resultados expressivos quanto à detecção de anticorpos IgM (≥ 30 unidades PANBIO). Os resultados obtidos no ELISA e *nested* PCR comprovaram a ocorrência de infecção recente em 5 das 8 CCs sob acompanhamento. Evidência sorológica de infecção recente para o vírus de Epstein-Barr (EBV) e parvovírus B19 foi identificada em 2,0% (8/401) e 1,5% (6/401) das crianças, respectivamente. Nossos resultados demonstram uma expressiva evidência de que o HHV-6 é uma causa comum de epidemias relacionadas a doença febril-exantemática em crianças matriculadas nas CCs da área urbana de Belém.

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