Hepatitis A Screening for Internationally Adopted Children From Hepatitis A Endemic Countries

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Abstract

Screening for hepatitis A virus (HAV) infection is not currently routinely recommended in internationally adopted children. International adoptees seen at the University of Minnesota International Adoption Clinic from 2006 to 2010 were assessed for acute HAV infection (positive HAV immunoglobulin M). Thirty of the 656 children screened (4.6%) were acutely HAV infected. HAV-infected children emigrated from Ethiopia (16), Guatemala (4), China (2), Colombia (2), Haiti (2), Philippines (2), Liberia (1), and Nepal (1). Infection was most frequent among children younger than 2 years (6.7%). No symptoms distinguished children with acute HAV infection from uninfected children. HAV infection caused significant social disruption, including separation of children from their ill adoptive parents during the initial weeks postarrival, a period important for postadoption adjustment and attachment. All international adoptees arriving from countries with high or intermediate HAV endemicity should be screened for HAV infection on arrival to the United States.

Keywords

hepatitis A, adoption, children

Introduction

Several previously published case series describe hepatitis A virus (HAV) infections among internationally adopted (IA) children and their contacts.[1-4] The Advisory Committee on Immunization Practices and American Academy of Pediatrics recently recommended that persons anticipating close contact with IA children within 60 days after arrival from a country with intermediate or high rates of HAV infection should be vaccinated against HAV.[5-7] Many IA children are adopted prior to the recommended age for HAV vaccination or come from countries that do not routinely immunize against HAV. Because the majority of IA children enter their families during early childhood, they are likely to be asymptomatic during acute HAV infection. The current American Academy of Pediatrics Red Book guidelines do not include HAV in the table of recommended routine screening tests for IA children, although the text mentions that this testing "can be performed" at the initial visit.[8]

Recently, Sweet et al[9] documented 10 secondary cases of HAV in Minnesota from 2007 to 2009 associated with exposure to HAV-infected IA children. That study identified 21 IA children with acute HAV infection during the study period, 12 of whom were identified through routine HAV screening at the University of Minnesota International Adoption Clinic (UMIAC).[9] In this article, we present 3 representative cases of acute HAV infection among IA children to highlight the social and family disruption that can be caused by isolation of the child from unimmunized persons and by infection passed from the asymptomatic child to unimmunized contacts. These cases led us to assess the frequency of acute HAV infection in IA children seen at the UMIAC and to determine whether factors such as country of origin, age, gender, or symptoms were associated with risk of acute HAV infection.

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Case Reports

Case 1

A 14-month-old Ethiopian boy was seen at the UMIAC. In Ethiopia, he lived with his biological parents for 9 months and in an orphanage for 2 months immediately prior to adoption. Except for occasional increased frequency of stools, the toddler had been well since arrival in the United States 9 weeks earlier. He attended a church nursery school weekly. Routine screening revealed that he was positive for HAV total antibody (testing for immunoglobulin G [IgG] or immunoglobulin M [IgM] antibodies to HAV) and follow-up testing revealed that he had HAV IgM but not IgG antibodies, demonstrating acute infection.

His adoptive mother reported his twin sister, adopted at the same time, tested positive for total HAV antibody at an outside clinic 4 weeks earlier, but was not ill and had not been tested for HAV IgM antibodies. The adoptive parents and an older sibling had been immunized against HAV prior to traveling to Ethiopia and remained well. At the time of the patient's visit to the UMIAC, the adoptive grandfather was acutely ill with HAV infection. He had not been immunized against HAV and had not traveled to Ethiopia but had contact with both children. A coworker of the HAV-infected grandfather also became seriously ill with HAV infection. Studies at the Minnesota Department of Health identified the virus shed in the toddler's stool to be identical to that shed by the grandfather and his coworker.

Case 2

A 12-month-old girl from Guatemala was brought to the UMIAC for her initial postadoption medical visit. Prior to adoption, she had lived in an orphanage since birth. Her adoptive parents reported that she had been well since arriving in the United States 3 months prior to the visit. Routine screening demonstrated that she was positive for total antibodies and IgM to HAV.

Her initial screening visit was delayed because both parents had become significantly ill shortly after the infant's arrival. They were subsequently diagnosed with HAV infection. Neither parent had been immunized against HAV prior to traveling to Guatemala. A first cousin, previously immunized against HAV, provided child care while the parents were ill in the critical first weeks of bonding for the child and parents. The child remained well.

Case 3

An 11-month-old male infant from Guatemala was brought to the UMIAC by his adoptive mother approximately 5 months postadoption with concerns of attachment problems and sleep disruption. He was seen by the family's pediatrician following his arrival in the United States at 6 months of age. His mother reported that the pediatrician did not screen for HAV. He was healthy during his initial pediatric examination and while living in a foster home prior to adoption. He developed symptoms of mild gastroenteritis approximately 2 to 3 weeks after his arrival.

One month after the child's illness, the mother became acutely ill with abdominal pain, nausea, vomiting, diarrhea, severe malaise, and neutropenia. She tested positive for acute HAV infection and was hospitalized in protective isolation for 1 week. She remained acutely ill for 6 weeks, during which the child was cared for by the adoptive father and maternal grandmother.

During the visit, the adoptive mother expressed grief that her relationship with her son had deteriorated during her hospitalization and convalescence. Exam at the clinic revealed active attachment behaviors of the child to his mother, but she remained concerned that her prolonged separation from her son resulted in impaired attachment during the early adoption period.

Methods

Electronic medical records of IA children seen at the UMIAC between January 1, 2006 and December 31, 2010 were examined. Inclusion criteria were as follows: documented informed consent for use of medical records for research, initial medical screening visit after arrival in the United States at the UMIAC, and documented results of HAV serology. The HAV serological testing consisted of screening for HAV total antibodies with a positive result automatically triggering evaluation for HAV IgM antibodies. Children were excluded if a HAV IgM antibody test was not performed following a positive total HAV antibody test or if only negative HAV IgM antibody results were available without the results of total HAV antibody testing. This allowed assessment of both immunity and presence of acute infection in all tested children. Children were categorized as susceptible, immune, or acutely infected based on their serology results. Susceptible children were defined by a negative test for total antibodies to HAV, immune children by a positive total HAV antibody test and negative test for HAV IgM antibodies, and acutely infected children by positive results for IgM antibodies to HAV.

Data on adoptees' gender, age at adoption, country of origin, arrival year, and symptoms if HAV IgM positive were collected. Logistic regression was used to compare odds of HAV infection between countries. Statistical analysis was conducted using STATA 10 (Stata Corporation, College Station, TX) and SAS (SAS

Institute Inc, Cary, NC). This study was approved by the University of Minnesota Institutional Review Board.

Results

Hepatitis A Screening

Hepatitis A serology was performed on 678 of 1428 children (47.5%) during their initial visit to the UMIAC from 2006 to 2010. Hepatitis A screening was performed at the discretion of the provider based on provider assessment of HAV risk. The percentage of adoptees screened for HAV increased yearly, from 5.4% in 2006 to 76.2% in 2010. This increase occurred as cases of documented HAV infection were seen in the UMIAC, prompting concern about potential missed cases of infection. Twenty-two children were excluded because they were positive for total HAV antibodies but lacked HAV IgM results (n = 8) or tested negative for HAV IgM without results for total HAV antibodies (n = 14), leaving 656 eligible children. These children represented 32 different countries, although 19 countries (Armenia, Democratic Republic of Congo, Ecuador, Ghana, Honduras, Iraq, Israel, Jamaica, Kyrgyzstan, Liberia, Mexico, Nepal, Romania, South Africa, Sri Lanka, St Vincent and the Grenadines, Taiwan, Uganda, Zambia) were represented by less than 5 adoptees. In all, 193 adoptees (29.4%) were from countries with high HAV endemicity, 114 adoptees (17.4%) were from countries with intermediate endemicity, and 349 adoptees (53.2%) were from countries with low to very low HAV endemicity.[7]

HAV Infection According to Country, Age, Gender, and Symptoms

Thirty children (4.6%, 95% confidence interval [CI] = 3.1-6.5) were acutely infected with HAV. Acutely infected children came from 8 countries: Ethiopia (16/166, 9.6%, 95% CI = 5.6-15.2), Guatemala (4/68, 5.9%, 95% CI = 1.6-14.4), China (2/113, 1.8%, 95% CI = 0.2-6.2), Colombia (2/27, 7.4%, 95% CI = 0.9-24.3), Haiti (2/27, 7.4%, 95% CI = 0.9-24.3), Philippines (2/13, 15.4%, 95% CI = 1.9-45.4), Liberia (1/4, 25%, 95% CI = 0.6-80.6), and Nepal (1/2, 50%, 95% CI = 1.6-98.7; Table 1). All these countries have been classified by the Centers for Disease Control and Prevention (CDC) as having intermediate or high hepatitis A endemicity with the exceptions of China and Haiti, which are classified as having low endemicity.[7] Odds ratios were not calculated for the risk of acute HAV infection by country because all countries except Ethiopia and Guatemala had 2 or fewer children with acute HAV infection.

Acute HAV infection was most common among adoptees in the youngest age-group (Table 1). Seventy-three percent of the adoptees with acute HAV infection were younger than 2 years. Among all international adoptees, 328 out of 656 (50%) were <2 years old. Among children from Ethiopia, 90/166 (54.2%) were <2 years old, and 10 of the 90 children <2 years old (11.1%) were HAV infected. Frequency of acute HAV infection did not differ by gender (Table 1).

Data on symptoms and signs were collected on 27 out of 30 adoptees (90%) with acute HAV infection. Seven (23.3%) of the acutely infected adoptees had diarrhea at the time of presentation. Six of the 7 children with diarrhea were from Ethiopia. The frequency of diarrheal symptoms in Ethiopian children with acute HAV infection (6/16 children, 37.5%) was actually lower than the frequency of diarrheal symptoms among Ethiopian children without HAV infection (60% in a subsample for which symptoms were available). Thus, diarrhea did not distinguish those with acute HAV infection from those without HAV infection. Other nonspecific symptoms noted among acutely HAV infected adoptees included 1 child each with abdominal distension, alternating diarrhea and constipation, and a history of recently resolved diarrhea. One child from Guatemala had hepatomegaly. The remaining 19 children with acute HAV infection had no symptoms or signs of acute infection.

Immunity to HAV According to Age, Country, and Gender

A total of 199 children (30.3%) were immune to HAV. Immunity to HAV was common among children aged 2 to 5 years (47.0%), aged 6 to 11 years (44.7%), and aged 12-17 years (73.7%), but much less frequent in children younger than 2 years (12.8%, Table 1). After adjustment for age, the odds of being HAV immune were significantly higher for children adopted from 6 countries: Guatemala, Colombia, Ethiopia, India, Ecuador, and Haiti compared with Korea, the baseline comparison country (Table 2). The odds of being HAV immune were not significantly different from those of the baseline comparison country for children from any other country (Table 2). Immunity to HAV did not differ according to gender (Table 1).

Discussion

In this study, we document that 4.6% of IA children screened for HAV infection were acutely infected with HAV. The prevalence of acute HAV infection among all IA children is likely lower since not all children were screened for HAV infection, but even if all children not

Table 1. Percentage of International Adoptees Who Were Hepatitis A Virus (HAV) Infected, Immune, or Susceptible, According to Country, Age, Gender, and Year.

	Total Number of Adoptees Tested for HAV	Number HAV Infected (%)	Number HAV Immune (%)	Number HAV Susceptible (%)
Gender				
Male	287	14 (4.9)	83 (28.9)	190 (66.2)
Female	369	16 (4.3)	116 (31.4)	237 (64.2)
Year				
2006	17	2 (11.8)	4 (23.5)	11 (64.7)
2007	142	9 (6.3)	54 (38.0)	79 (55.6)
2008	139	9 (6.5)	28 (20.1)	102 (73.4)
2009	160	3 (1.9)	41 (25.6)	116 (72.5)
2010	198	7 (3.5)	72 (36.4)	119 (60.7)
Country				
Armenia	1	0	0	1 (100)
China	113	2 (1.8)	19 (16.8)	92 (81.4)
Colombia	27	2 (7.4)	16 (59.3)	9 (33.3)
Democratic Republic of Congo	3	0	0	3 (100)
Ecuador	4	0	3 (75)	1 (25)
Ethiopia	166	16 (9.6)	83 (50)	67 (40.4)
Ghana	1	0	0	1 (100)
Guatemala	68	4 (5.9)	19 (27.9)	45 (66.2)
Haiti	27	2 (7.4)	18 (66.7)	7 (25.9)
Honduras	1	0	1 (100)	0
India	11	0	7 (63.6)	4 (36.4)
Iraq	1	0	0	1 (100)
Israel	1	0	0	1 (100)
Jamaica	1	0	0	1 (100)
Kazakhstan	10	0	4 (40)	6 (60)
Korea	50	0	1 (2)	49 (98)
Kyrgyzstan	1	0	0	1 (100)
Liberia	4	1 (25)	2 (50)	1 (25)
Mexico	1	0	0	1 (100)
Nepal	2	1 (50)	1 (50)	0
Philippines	13	2 (15.4)	1 (7.7)	10 (76.9)
Romania	1	0	1 (100)	0
Russia	98	0	17 (17.3)	81 (82.7)
South Africa	2	0	2 (100)	0
Sri Lanka	1	0	0	1 (100)
St Vincent and the Grenadines	1	0	0	1 (100)
Taiwan	1	0	0	1 (100)
Thailand	5	0	0	5 (100)
Uganda	3	0	3 (100)	0
Ukraine	25	0	0	25 (100)
Vietnam	12	0	0	12 (100)
Zambia	1	0	1 (100)	0
Age (years)				
<2	328	22 (6.7)	42 (12.8)	264 (80.5)
2-5	215	5 (2.3)	101 (47.0)	109 (50.7)
6-11	94	2 (2.1)	42 (44.7)	50 (53.2)
12-17	19	1 (5.3)	14 (73.7)	4 (21.0)
Overall	656	30 (4.6)	199 (30.3)	427 (65.1)

Table 2. Odds Ratios for Immunity to Hepatitis A Virus by Country.

Country	Odds Ratio[a]	95% Confidence Interval	*P*
China	5.9	0.8-46.0	.09
Colombia	39.6	4.5-347.4	.001
Ecuador	54.6	2.6-1148.6	.01
Ethiopia	39.9	5.3-298.1	<.001
Guatemala	15.5	2.0-121.4	.009
Haiti	37.3	4.1-341.4	.001
India	30.2	2.8-321.8	.005
Kazakhstan	9.1	0.8-107.5	.07
Liberia	37.4	1.3-1084.9	.03
Philippines	1.2	0.1-23.0	.9
Russia	2.3	0.3-19.3	.44
South Korea[b]	1	—	—
Other	1.7	0.1-34.8	.73

[a]Odds calculated by logistic regression, adjusted for age.
[b]Baseline comparison country. Immunity was present in 1 out of 50 adoptees screened from South Korea. South Korea was chosen as the baseline country because it was the country with the lowest immunity rate, so could be give a baseline odds ratio of 1.

screened were HAV negative, the prevalence would still be high (2.1%). Our study findings add to those of a recent study on HAV infection in IA children in Minnesota[9] by assessing IA children seen over a 5-year period, documenting several additional countries with a high risk of adoptees with HAV infection, providing an estimate of minimum prevalence of acute HAV infection in IA children seen at the UMAIC, and demonstrating the significant social and medical disruption that acute HAV infection of an IA child can lead to among families and contacts, including separation of the child from one or both parents during the first weeks after arrival, a critical period for adjustment and attachment for these children.

To place our findings in a local perspective, 174 cases of HAV were reported to the Minnesota Department of Health from 2006 to 2008.[10-12] Twenty IA children evaluated at UMIAC during this time period were acutely infected with HAV, representing 11.5% of all reported HAV infections in Minnesota during these 3 years. Thus, IA children represent a major risk group for HAV infection in Minnesota and were the source (as documented in part in the case studies in this manuscript) of several additional cases of acute HAV infection in Minnesota.

The prevalence of acute HAV infection was highest in children adopted from Ethiopia (n = 16, 9.6%). All adoptees found to be acutely infected emigrated from countries classified by the CDC as having intermediate or high HAV endemicity with the exception of 4 adoptees (13.3%) from China and Haiti, which are classified as low endemicity countries.[7] The 2 adoptees from Haiti with acute HAV infection arrived within 4 months of a 7.0 magnitude earthquake in Haiti, which led to large-scale damage and disruption of infrastructure. It is possible that the disruption to sanitation in the aftermath of this earthquake led to a temporary increase in hepatitis A endemicity in Haiti during this time frame, though to our knowledge, no published data exist to support this theory. Limiting HAV screening of IA children to children from countries of intermediate- to high-endemicity, countries suffering from large-scale sanitation disruptions such as natural disasters, and China would have captured all children with HAV infection. No children from other low or very low HAV endemicity by CDC criteria had HAV infection (0 out of 210, 95% CI = 0.0% to 1.7), suggesting that screening from countries, such as Russia, the Ukraine, and South Korea, may be unnecessary under normal circumstances.

Seventy-three percent of acute HAV infections were among adoptees younger than 2 years. This likely represents early exposure to HAV in areas of high endemicity after maternal antibodies wane. Passively acquired maternal anti-HAV antibodies diminish over the first year of life, with between 36.1%[13] and 61.1%[14] of infants having protective levels at 12 months. Maternal antibodies may account for some of the cases of immunity seen among children younger than 1 year. Of note, there were no symptoms or physical exam signs that distinguished children with HAV infection from those without it, highlighting the importance of screening all at-risk children regardless of symptoms.

Testing for acute HAV infection by anti-HAV IgM is the standard endorsed by the American Academy of Pediatrics[8] and is the most practical screening method available. There can be a window period in which a person is HAV infected but does not have IgM antibodies to HAV,[15] so the test should be repeated in symptomatic individuals in whom HAV infection is suspected if HAV IgM is initially negative. It is possible that some children with acute HAV infection were missed on initial testing in our study, but the UMIAC and the Minnesota Department of Health documented no cases of HAV infection spread from an IA child who tested HAV IgM negative. Newer methods of serum testing by polymerase chain reaction, including real-time polymerase chain reaction, have been proposed[16,17] and may be more accurate during the window period. They hold promise for future testing but are not currently validated as screening measures.

A recent article from Cincinnati Children's Hospital Medical Center (CCHMC) documented acute HAV infection in only 1% of adoptees seen at their international adoption clinic.[18] That study presented results from children screened for HAV infection, as did the present study, but had a study population less than half

the size of the present study (CCHMC, n = 288; UMIAC, n = 656). In the CCHMC study, there were far fewer children from Ethiopia (n = 24) as compared with the present study (n = 166), but even if children from Ethiopia were excluded, the acute HAV infection rate in the UMIAC population would be 2.9% (14/490 children), nearly triple the 1% seen at CCHMC. In Ethiopian adoptees at the UMIAC, there was a high rate of acute HAV infection (9.6%), whereas none of the children from Ethiopia seen at CCHMC were acutely HAV infected. Age was likely a factor in the difference in prevalence of HAV infection in the CCHMC and UMIAC children adopted from Ethiopia. Children younger than 2 years comprised 73% of all children with acute HAV infection and 62.5% of Ethiopian children with HAV infection (10 of 16) in the current study and the UMIAC had a higher frequency of Ethiopian children younger than 2 years (90 of 166, 54.2%) than CCHMC (37.5%). Other potential reasons for these discrepancies include differences in screening parameters (eg, the UMIAC may have screened more children and thus detected more asymptomatic infections) or differences in the sanitary conditions in the care settings from which Ethiopian adoptees were living prior to adoption.

Hepatitis A immunization is recommended for all children. However, a significant number of IA children (30.3% in this study) have immunity from a prior natural infection and do not require the vaccine. This population can easily be identified by initial screening for total HAV antibodies and testing only those with total antibodies for IgM antibodies to differentiate immunity from acute HAV infection. A small number of IA children are acutely infected with HAV and infected children can continue to shed the virus for several days after immunization.[7,19] Early screening can save immunization costs and time for children who are already immune and knowledge of HAV infection in an adopted child can lead to appropriate precautions and potentially halt the spread of infection to others. For these reasons, we believe that screening for HAV infection in children from countries of intermediate to high hepatitis A endemicity and low-endemicity countries experiencing large-scale disruptions in sanitation is important even though most IA children will ultimately require the hepatitis A vaccination.

In a recent article on acute HAV infection in IA children in Minnesota, Sweet et al[9] identified that 38% of HAV-infected IA children were linked to subsequent HAV cases. The case studies presented in this report document for the first time how acute HAV infection in the child, often accompanied by spread of infection to relatives or caregivers, can lead to significant interruption of care of the newly adopted child by his or her adoptive parents during the critical first weeks after arrival. Interruption of care due to family member illness, especially in the initial adoption period, poses a significant threat to family–child postadoption adjustment. Experts in international adoption stress that parents should minimize the number of caregivers and focus on providing consistent, responsive, and sensitive care for their newly adopted child during the initial weeks and months following arrival.[20(pp353-368),21,22] The vast majority of children seen at the UMIAC lived in an orphanage prior to their adoption; for example, approximately 90% of children from Ethiopia, the country with the highest rate of acute HAV infection, lived in an orphanage prior to adoption (JKE, unpublished data). Children living in institutional care for 6 months or more are at risk for parent–child attachment difficulties, as these children rarely receive the sensitive, individualized, responsive care that is predictive of parent–child attachment relationship quality.[23-26] Additionally, most children adopted from orphanage care come to their families after the age of 9 to 12 months, when children have typically already established an attachment relationship with a primary caregiver.[27] For adoptive parents receiving children at this vulnerable age, prevention of illness and maintenance of health stamina is of paramount importance for their new adopted children and for themselves. Previous reports have recorded that HAV infection spread from the infected adopted child to caregivers or contacts, but the case reports in the present study provide the first documentation of the separation of the child from his or her parents during the initial weeks postadoption. The third case report also highlights for the first time the considerable emotional toll this separation took on a child's adoptive parent. These additional social and attachment considerations provide further basis for acute HAV testing in all children from areas of moderate or high HAV endemicity.

Conclusion

The prevalence of active HAV infection among IA children was 4.6%, indicating that HAV infection is not uncommon among IA children. These findings support testing for acute HAV infection in all international adoptees arriving from countries with high or intermediate HAV endemicity, as well as in children from China, which is now classified as having low HAV endemicity, and children adopted from situations that may disrupt normal sanitation conditions (eg, natural disasters). Detecting active HAV infection will allow preventive measures to limit fecal–oral contamination, reduce the number of persons exposed (eg, avoidance of daycare), and allow passive prophylaxis to be administered in a timely manner to nonvaccinated individuals who have had close contact with the child.

Our experiences also support the new Advisory Committee on Immunization Practices and American Academy of Pediatrics guidelines that all persons anticipating close contact with an international adoptee within 60 days of arrival be vaccinated against HAV.[5-7] Prevention of spread of HAV to adoptive parents and extended family members is the primary benefit of the new immunization recommendations, but preventing disruption of family–child postadoption adjustment is an important secondary benefit.

Declaration of Conflicting Interests

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