Original Article

Evaluation of pediatric patients with hepatitis A

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Abstract

Introduction: Hepatitis A is the most common form of acute viral hepatitis worldwide, especially in children. The clinical severity of the hepatitis A virus (HAV) infection varies from an asymptomatic infection to a fulminant disease. In this study, we aimed to evaluate characteristics of pediatric patients diagnosed with HAV infection.

Methodology: Patients younger than 18 years of age admitted between January 1, 2006 and January 1, 2011 to our hospital, an important reference center located in the middle part of Turkey, diagnosed as having hepatitis A were evaluated.

Results: Of 427 patients, 49.4% were female and 50.6% were male. Hospitalization rate of the patients was 28.3%. The reason for hospitalization was vomitting in 58.7% of the patients and abdominal pain in 28%. The mean time of hospitalization was 5.2 ± 4.5 (1–40) days. There was no significant difference in hospitalization time by age. Vomiting and abdominal pain were significantly more common, and PT and aPTT levels were significantly elevated in patients with elevated AST and ALT levels over 1000 IU/L ($p < 0.001$). PT elevation was present in 15.2% of the patients, aPTT elevation in 11.9%, leukopenia in 16.6%, and thrombocytopenia in 2.6%. In terms of atypical course, four patients (0.9%) had cholestatic hepatitis, one had recurrent hepatitis, and one had fulminant hepatitis, yet no mortality was observed.

Conclusions: Atypical courses of hepatitis A were more scarce in pediatric patients, but careful follow-up of patients with AST and ALT levels > 1000 IU/L is necessary.

Key words: hepatitis A; pediatric; fulminant; cholestatic

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Introduction

Hepatitis A is generally an acute, self-limiting liver infection transmitted through the faecal-oral route by a picornavirus, the hepatitis A virus (HAV), which causes 10 million infections worldwide each year [1,2]. The clinical spectrum ranges from mostly asymptomatic infection to rarely fulminant hepatitis [3,4], and age is the major factor that influences the clinical course of the primary HAV infection; it is symptomatic in only 4%–16% of children compared to 75%–95% of adults. The degree of endemicity is closely related to the prevailing hygiene and sanitary conditions, socio-economic level, vaccination, and other development indicators [5]. In Turkey, a country with intermediate endemicity for HAV, seropositivity has been found to vary according to the geographical area. It has been found to be more commonly positive in earlier ages in eastern Anatolia compared to western parts [6,7]. In this study, we aimed to overview the characteristics and outcomes of the pediatric patients diagnosed with HAV infection.

Methodology

In this study, pediatric patients younger than 18 years of age admitted between January 1, 2006 and January 1, 2011 to our hospital, an important reference center located in the middle part of Turkey, diagnosed as having hepatitis A were evaluated retrospectively. Patients with negative anti-HAV IgM were excluded from the study. Data analysis included age, gender, household size, symptoms, laboratory studies (hemogram, C reactive protein, sedimentation rate, biochemical studies, prothrombin [PT] and activated thromboplastin time [aPTT]), hospitalization period (if present), complication (if present), and outcome of the patient. An atypical course of HAV was categorised as cholestatic hepatitis, recurrent hepatitis, and fulminant hepatitis. Cholestatic hepatitis was defined as direct bilirubin level higher than 50% of total bilirubin level and total bilirubin level higher than 10 mg/dl over a four-week period. Recurrent hepatitis was defined as recurrence in high levels of liver function tests one to four months following partial or total recovery in transaminases and observation of bilirubin levels with

ongoing anti-HAV IgM positivity. Fulminant hepatitis was defined as worsening of icterus, liver functions and presence of hepatic encephalopathy in a two-week period.

Statistical analysis was performed with the Statistical Package for the Social Sciences version 17.0 (SPSS, Microsoft Inc. Chicago, USA,). Continuous variables are described as arithmetical means with standard deviations (SD). Student's *t*-test was used for comparison of continuous variables between two groups. Categorical variables are described as absolute frequencies and proportions. A p value of 0.05 was considered statistically significant.

Results

Of 427 patients diagnosed with HAV infection, 49.4% were female and 50.6% were male. The mean age of the patients was 8.7 ± 3.5 (1–17) years. Distribution according to age and gender is reported in Table 1. A total of 64.4% of children lived in shanty houses, 35% did not have access to an indoor lavatory, 70% lived in households of five people or more, and 28.5% had close contact with hepatitis A. Patients' complaints are summarized in Table 2. Abdominal pain, jaundice, dark urine, light-colored stool, arthralgia, myalgia, and pruritus were more common in children between 13 and 17 years of age, whereas diarrhea was more common in children between 1 and 4 years of age. Physical examination of the patients yielded icterus in 76.8%, hepatomegaly in 56.7%, hypotension in 33.7%, fever in 16.4%, and splenomegaly in 11%.

Laboratory studies yielded leukopenia in 16.6%, leukocytosis in 12.7%, thrombocytopenia in 2.6%, and thrombocytosis in 7.7%. Other laboratory studies are shown in Table 3. Of the patients in the 13-17 age group, 69.7% had aspartate aminotransferase (AST) levels higher than 1000 U/L, and 77.3% had alanine aminotransferase (ALT) levels higher than 1000 U/L. The relationships between age and AST and ALT levels were parallel ($p < 0.001$). Patients with ALT and AST levels higher than 1000 U/L had vomiting ($p < 0.001$) and abdominal pain ($p < 0.001$) significantly more commonly. Hypoglycemia was significantly more common in patients with ALT ≥ 1000 U/L ($p < 0.01$).

The hospitalization rate of the patients was 28.3%. The most common causes of the hospitalization were vomiting (58.7%) and abdominal pain (28%). The average hospital stay due to hepatitis A was 5.2 ± 4.5 (1–40) days. There was no significant difference in hospitalization rates between the age groups. There was positive correlation between ALT levels and total bilirubin, direct bilirubin, PT, aPTT, and hospitalization periods (OR = 0.374, O R= 0.382, OR = 0.470, OR = 0.253, OR = 0.248, respectively; $p <$ 0,001 for all). Also, there was positive corelation between AST levels and ALT, total bilirubin, direct bilirubin, PT, aPTT and hospitalization periods (respectively, r = 0.833, r = 0.264, r = 0.272, r = 0.417, r = 0.178, r = 0.187; $p <$ 0,001 for all). There was also positive correlation between total and direct bilirubin levels and PT, aPTT, and hospitalization periods (respectively, r = 0.973/0.381, r = 0.368/0.186, r = 0.326/0.288; $p < 0.001$ for all). Elevation in PT levels increased hospitalization risk nine times (OR = 9.265), whereas increase in aPTT levels caused a fivefold higher risk of hospitalization (OR = 5.43). There was positive correlation between PT levels and aPTT levels and length of hospital stay (r = 0.385, r = 0.357; $p < 0.001$ for all). Also, aPTT levels were positively related with length of hospital stay (r = 0.141; $p <$ 0.01).

In terms of atypical course, four patients (0.9%) had cholestatic hepatitis, one patient had recurrent hepatitis, and one patient had fulminant hepatitis, yet no mortality was observed. The patient with fulminant hepatitis underwent liver transplantation sucessfully.

Discussion

HAV infection is common throughout the developing world, where infections most frequently are acquired during early childhood. In developed countries, HAV infection is less common, but community-wide outbreaks may occur. Turkey has been defined as intermediately endemic for hepatitis A infection [8].

HAV infection is most common in children under 15 years of age and is distributed equally among genders. In a study reported from Argentina [9], the mean age of 288 children was 6.9 ± 3.5 (1.5–14) years, and in a study from Turkey evaluating 221 pediatric patients, the mean age was 9.12 ± 3.65 (1.5–16.5) years [10]. In our study, 92.5% of the patients were younger than 15 years; the mean age was 8.7 ± 3.5 (1–17) years, similar to the other studies. Male/female ditribution was equal. After age of nine, however, HAV infection was more common in the male population, which might be due to increased exposure of boys to social life depending of socio-economic circumstances in Turkey.

Table 1. Distribution according to age and gender

Age groups (years)	Gender			
	Female		Male	
	n	%	n	%
1–4	32	56.1	25	43.9
5–8	85	53.1	75	46.9
9–12	64	44.4	80	55.6
13–17	30	45.5	36	54.5

Table 2. Distribution of complaints according to age group

Complaint	Age group				P	Total
	1–4 yrs	5–8 yrs	9–12 yrs	13–17 yrs		
	%	%	%	%		%
Lack of appetite	92.9	92.5	90.2	95.4	p > 0.05	92.2
Malaise	89.4	88.1	92.3	93.9	p > 0.05	90.6
Nausea	80.7	78.7	77.7	90.9	p > 0.05	80.5
Abdominal pain	80.7	78.7	77.7	90.9	**p < 0.001**	77
Icterus	45.6	70	80.5	92.4	**p < 0.001**	73.7
Dark urine	26.3	53.1	67.3	75.7	**p < 0.001**	57.8
Vomiting	71.9	55.6	53.4	54.5	p > 0.05	56.9
Arthralgia/myalgia	0	20.6	43	66.6	**p < 0.001**	32.5
Fever	26.3	25	21.5	27.2	p > 0.05	24.3
Light-colored stool	1.8	15	20.8	40.9	**p < 0.001**	19.2
Pruritus	5.2	11.8	18	42.4	**p < 0.01**	17.7
Constipation	22.8	17.5	15.2	10.6	p > 0.05	16.3
Diarrhea	28	7.5	7.6	9	**p < 0.001**	10.5
Epistaxis	1.7	3.1	3.4	1.5	p > 0.05	2.8
Ecchymosis	0	0.6	0	0	-	0.2

Table 3. Laboratory studies

Label	Mean ± standard deviation (min-max.)
AST (U/L)	1,053 ± 809 (23–5,520)
ALT (U/L)	1,172 ± 743 (11–3,923)
Total bilirubin (mg/dL)	5.1 ± 3.1 (0.25–26.2)
Direct bilirubin (mg/dL)	3.7 ± 2.4 (0.03–17.9)
Glucose (mg/dL)	91.7 ± 17.3 (50–164)
Albumin (gr/dL)	3.8 ± 0.5 (2.4–5.5)
ALP (U/L)	817 ± 439 (55–2664)
GGT (U/L)	109 ± 89.8 (5–690)
BUN (mg/dL)	25.4 ± 8.9 (3–56)
Na (mEq/L)	135 ± 3.3 (127–145)
K (mEq/L)	3.8 ± 0.4 (3–5.9)
Sedimentation rate (mm/hour)	20.2 ± 11.4 (2–74)
CRP (mg/dL)	0.92 ± 1 (0.06–12)

The association of HAV infection risk with standards of hygiene and sanitation and the age-dependent clinical expression of the disease determine the different patterns of HAV infection observed worldwide [11]. In a study from Turkey, it was reported that HAV seroprevalance was higher in children living in shanty houses without access to an indoor lavatory, compared to children living in apartments with an indoor lavatory [12]. In our study, 70% of children lived in households with five or more people, 64.4 % lived in shanty houses, and 35% did not have access to an indoor lavatory.

Of the patients diagnosed with HAV, 45% were reported to have had close contact with an HAV-infected person, and secondary HAV infection was noted in 54% [12]. In our study, 28.5% of the patients had had close contact with an HAV-infected person. These results emphasize the importance of preventive measures when a case with HAV is detected.

Age is the major factor influencing the clinical course of the primary HAV infection [13], and it has been documented that > 70% of children younger than six years of age have asymptomatic HAV infections, whereas 20% of children older than six years of age have asymptomatic infections [14]. Similarly in our study, adolescent patients between 13 and 17 years of age were more commonly symptomatic, having abdominal pain, icterus, dark urine, light-colored stool, myalgia, athralgia, and pruritus.

In a previous study [15], physical examination of HAV-infected patients yielded, most commonly, hepatomegaly and splenomegaly, similar to the findings in our study; 56.7% had hepatomegaly and 11% had splenomegaly. Hospitalization rates of HAV-infected patients were 42.1% in Spain, 33% in USA [16], and 28.3% in our study. The hospitalization period was 6.8 days in Spain and 6.7 days in Korea [17] compared to 5.2 ± 4.5 days in our study.

The course of HAV infection could be atypical in forms of cholestatic, recurrent, or fulminant hepatitis, with a percentage of 7% (9). In our study, this percentage was lower (1.4%), which might be due to acquisition of HAV in younger ages asymptomatically in Turkey compared to less endemic countries.

Elevation in ALT and AST levels is one of the first signs of hepatocellular inflammation and liver injury. In our study, patients with AST and ALT levels higher than 1000 U/L had a worsening in clinical findings and required longer hospitalization periods, showing that these patients should be monitored closely.

Safe and effective inactivated hepatitis A vaccines have been available since 1992 worldwide. National immunization programs have been successful, with good coverage rates and declines in incidence of up to 90%. Countries that have implemented universal immunization have demonstrated a successful impact on the incidence of hepatitis A; the data for the United States is particularly striking, with evidence of a two-thirds decrease in admissions to hospital and markedly lower medical expenditures between 1996 and 2004 [18]. Since November 2012, the hepatitis A vaccine was implemented in the national vaccination schedule of Turkey. In our study, patients admitted to one of the largest pediatric hospital in our country were evaluated to gather data about the status of HAV infection in Turkey. With this study, the importance of preventive measures and vaccination became evident, as hygienic conditions and other indicators of the level of socio-economic development in Turkey are not yet fully sufficient.

In conclusion, we was observed that an atypical course of hepatitis A was more scarce in pediatric patients, but careful follow-up of patients with elevated levels of AST and ALT levels higher than 1000 IU/L is necessary.

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