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Clinical Manifestations, Laboratory Findings and Disease Course of Iranian Pediatric Patients Diagnosed with Hepatitis A Infection

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Abstract

Background: According to some provincial reports, prevalence of hepatitis A has had a decreasing trend during the past decade in Iran. We aimed to overview clinical manifestations and laboratory findings of Iranian pediatric patients diagnosed with hepatitis A infection. **Materials and Methods:** This retrospective study was performed on 162 consecutive pediatric cases of hepatitis A infection. Data were collected by reviewing hospital records on admission to hospital.**Results:** The mean±SD age of participants was 9.90±4.08 years and 55.6% were boys. Regarding clinical manifestations, the most frequent symptom was jaundice. Fever was more prevalent in girls than in boys; whereas, abdominal tenderness was more prevalent in boys compared to girls. There was no difference in the prevalence of other clinical indices as well as in laboratory parameters between two sexes. Diarrhea was significantly more frequent in children younger than 2 years compared with other age subgroups. However, abdominal tenderness was more frequent in older patients compared to younger children. Regarding laboratory parameters, except for serum direct bilirubin that raised less in children younger than 2 years, the prevalence of other biochemical markers abnormality was comparable in different age groups. **Conclusion:** Hepatitis A infection is a common finding among Iranian children that equally occurs in boys and girls, while commonly appearing in children aged 7-18 years. The most frequent abnormal changes in laboratory parameters refer to change of liver enzymes, serum bilirubin, serum albumin and coagulated indices. **[GMJ.2015;4(2):90-95]**

Keywords: Hepatitis A; Clinical Manifestation; Laboratory Findings; Children

Introduction

Recent development in serological testing and accurate molecular techniques have led to greater knowledge and understanding of the nature, methods of transmissions, mechanisms of vaccination, epidemiological characteristics and geographical distribution of viruses [1, 2]. This scientific development successfully resulted in performing appropriate global immunization programs as well as controlling viral epidemics in both developing and colony countries [3, 4]. In this regard, the incidence rate of viral infections is considerably different according to socioeconomic status, sanitary provision observance, planning appropriate health policies and especially quality of prevailing vaccination [5].

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During recent decades, successful immunization against hepatitis A as an acute and self-limiting liver infection has led to controlling the incidence rate of this infection and also its rare life-threatening complications such as fulminant hepatitis [6-8]. This viral infection can appear in both children and adults, but with different clinical symptoms and final clinical consequences. Classical manifestations of hepatitis A are less likely in young patients with asymptomatic feature, while in adults, it can manifest in clinical symptoms and also adverse events such as fulminant hepatitis [9, 10]. Thus, age is the major factor that affects the clinical course of this disease. Disease progression is more severe in adults than in children; however, because hepatitis A is mostly asymptomatic or with non-specific manifestations, it may have a latent nature remaining indistinguishable from other bacterial and viral infections [11]. Moreover, the epidemiological picture of hepatitis A and also its-related age ratio may change over time, emphasizing changes in prevention and control policies in each society [12]. These augments accentuate to identify epidemiological characteristics of hepatitis A among children to more appropriately prevent its unfavorable clinical outcome.

Iran is a developing country with intermediate endemicity for hepatitis A and various sero-positivity according to geographical areas. Fortunately, serum prevalence of hepatitis A has had a decreasing trend during the past decade in our country according to some provincial reports; however, no comprehensive study is available on the clinical and epidemiological picture of hepatitis A among Iranian children. In the current study, we aimed to overview clinical manifestations, laboratory findings and disease course of Iranian pediatric patients diagnosed with hepatitis A infection.

Materials and Methods

This retrospective study was performed on 162 consecutive pediatric cases of hepatitis A infection younger than 18 years of age admitted between 2006 and 2011 to Namazi and Dastgheib hospitals. Diagnosis was based on anti-HAV IgM (Delawer, USA and Vidas kit, France) positivity and thus those with negative test results were excluded from this study. The study data were collected by reviewing hospital recorded files including demographics, laboratory parameters and clinical manifestations on admission to the hospital. 38 patients with incomplete data were not included in the final analysis. The collected data were then entered into an electronic database and preprogrammed consistency checks to minimize transcription errors. The distribution of study parameters was finally analyzed and reported according to sex and different age group categorizations. The study protocol was approved by the research committee at Shiraz University of Medical Sciences.

Results were presented as mean±standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. Continuous variables were compared with t-test or Mann-Whitney U-test whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the study groups. Categorical variables were, on the other hand, compared using chi-square test. For the statistical analysis, SPSS software, version 20.0 for windows (SPSS Inc., Chicago, IL) was used. P-values of 0.05 or less were considered statistically significant.

Results

Of total, 162 children aged younger than 18 years were assessed with respect to sex and age distribution of both clinical and paraclinical indices of hepatitis A infection. Mean±SD age of the participants was 9.90±4.08 and 55.6% were boys. Regarding clinical manifestations, the most frequent symptom was jaundice (76.5%) followed by repeated vomiting (72.2%), abdominal pain (61.1%), fever (59.9%) and abdominal tenderness (50.6%). Less common findings also included hepatomegaly (42.6%), malaise (16.0%), diarrhea (11.7%), itching (4.9%), encephalopathy (4.9%) and ascites (4.3%). The abnormal elevation of liver enzymes (more than two times of normal) was observed in 98.8% of chil-

dren; while the rise of total and direct serum bilirubin (total bilirubin >1 and direct bilirubin >0/5) was observed in 99.4% and 96.3%, respectively. In addition, 12.3% experienced hypoalbuminemia (<3/4mg/dl). Pancytopenia (WBC <4000 and Hb <10.5 and Plt <84000) was shown in only 1.2%. A notable number of patients experienced hemolysis evidences (80.9%). Regarding coagulative changes, abnormal PT (>15) and INR (>1) was also seen in 21.0% and 59.3% of subjects, respectively. However, a few children suffered from hypoglycemia (<50) (0.6%).

As shown in table1, comparing clinical manifestations of hepatitis A between boys and girls showed higher prevalence of fever in girls than in boys (54.6% versus 45.4%, P=0.001), whereas abdominal tenderness was more prevalent in boys compared with girls (63.4% versus 36.6%, P=0.042). There was no difference in prevalence of other clinical indices between two genders. In addition, no significant difference was revealed in laboratory biomarkers between boys and girls.

Table 2 compares clinical and paraclinical characteristics of hepatitis A infection across three age subgroups including 0-2 years, 3-6 years and 7-18 years. In this regard, diarrhea was significantly more frequent in children younger than 2 years compared with other age subgroups (66.7% in 0 to 2 years of age, 14.7% in 3 to 6 years of age and 9.6% in 7 to 18 years of age, p=0.008). However, abdominal tenderness was more frequent in older compared to younger children (33.3% in 0 to 2 years of age, 29.4% in 3 to 6 years of age and 56.8% in 7 to 18 years of age, P=0.015).

Table 1. Clinical and paraclinical status of hepatitis A total and in male and female patients

Characteristics	Total (n = 162)	Boys (n = 90)	Girls (n = 72)	P value
Clinical parameters				
Fever	97 (59.9)	44 (45.4)	53 (54.6)	0.001
Repeated vomiting	117 (72.2)	67 (57.3)	50 (42.7)	0.480
Jaundice	124 (76.5)	70 (56.5)	54 (43.5)	0.678
Diarrhea	19 (11.7)	13 (68.4)	6 (31.6)	0.230
Malaise	26 (16.0)	17 (65.4)	9 (34.6)	0.271
Abdomen pain	99 (61.1)	49 (49.5)	50 (50.5)	0.052
Abdomen tenderness	82 (50.6)	52 (63.4)	30 (36.6)	0.042
Hepatomegaly	69 (42.6)	41 (59.4)	28 (40.6)	0.394
Itching	8 (4.9)	5 (62.5)	3 (37.5)	0.685
Ascites	7 (4.3)	3 (42.9)	4 (57.1)	0.489
Encephalopathy	8 (4.9)	4 (50.0)	4 (50.0)	1.000
Anorexia	61 (37.7)	35 (57.4)	26 (42.6)	0.717
Lab. Parameters				
AST rise	160 (98.8)	89 (55.6)	71 (44.4)	0.874
ALT rise	160 (98.8)	88 (55.0)	72 (45.0)	0.203
Total bilirubin rise	161 (99.4)	89 (55.3)	72 (44.7)	0.370
Direct bilirubin rise	156 (96.3)	86 (55.1)	70 (44.9)	0.577
Abnormal albumin	20 (12.3)	9 (45.0)	11 (55.0)	0.310
Pancytopenia	8 (1.2)	1 (50.0)	1 (50.0)	1.000
Hemolysis	131 (80.9)	77 (58.8)	54 (41.2)	0.090
Abnormal PT	34 (21.0)	18 (52.9)	16 (47.1)	0.730
Abnormal INR	96 (59.3)	55 (57.3)	41 (42.7)	0.592
Hypoglycemia	1 (0.6)	1 (100)	0 (0.0)	0.370

Regarding laboratory parameters, except for serum direct bilirubin that was raised less in children younger than 2 years compared with other age subgroups, the prevalence of other biochemical markers abnormality were comparable in these three age groups (Table 2).

Discussion

The main points of the present study are that the prevalence of hepatitis A infection hospitalized in our population is similar in boys and girls; however, it is interestingly less detected in younger children, so almost 78% of affected ones are in the range of 7-18 years, while only less than 0.2% of infected children are younger than 2 years. This finding is considerably important because although the risk for occurring hepatitis A is similar in both genders among hospitalized patients, its risk is higher in older children and adults and thus the risk for its adverse consequences seems to be higher in older population. The second point is that almost all studied children suffered from at least one clinical symptom related to hepatitis A infection and therefore asymptomatic state was rarely reported in hospitalized patients. It has been clearly shown that the clinical spectrum of hepatitis A in children range from asymptomatic status in most subjects to rare encephalopathy and fulminant hepatitis. In fact, the clinical features of this disease are potentially dependent on the patient's age so that older patients face more dominant clinical manifestations.

According to our observations, the mean age of affected patients was 9.9 years and most prevalent in children aged 7-18 years.

Table 2. Clinical and Paraclinical Status of Hepatitis A Total and in Different Age Groups

Characteristics	0-2 years (n = 3)	3-6 years (n = 34)	7-18 years (n = 125)	P value
Clinical parameters				
Fever	3 (100)	18 (52.9)	76 (60.8)	0.255
Repeated vomiting	3 (100)	21 (61.8)	93 (74.4)	0.192
Jaundice	2 (66.7)	27 (79.4)	95 (76.0)	0.925
Diarrhea	2 (66.7)	5 (14.7)	12 (9.6)	0.008
Malaise	0 (0.0)	8 (23.6)	18 (14.4)	0.327
Abdomen pain	2 (66.7)	24 (70.6)	73 (58.4)	0.425
Abdomen tenderness	1 (33.3)	10 (29.4)	71 (56.8)	0.015
Hepatomegaly	1 (33.3)	19 (55.9)	49 (39.2)	0.207
Itching	0 (0.0)	0 (0.0)	8 (6.4)	0.288
Ascites	0 (0.0)	4 (11.8)	3 (2.4)	0.055
Encephalopathy	0 (0.0)	2 (5.9)	6 (4.8)	0.893
Anorexia	2 (66.7)	11 (32.4)	48 (38.4)	0.469
Lab. Parameters				
AST rise	3 (100)	33 (97.1)	124 (99.2)	0.594
ALT rise	3 (100)	33 (97.1)	124 (99.2)	0.594
Total bilirubin rise	3 (100)	34 (100)	124 (99.2)	0.862
Direct bilirubin rise	2 (66.7)	34 (100)	120 (96.0)	0.013
Abnormal albumin	0 (0.0)	7 (20.6)	13 (10.4)	0.224
Pancytopenia	0 (0.0)	0 (0.0)	2 (1.6)	0.741
Hemolysis	2 (66.7)	25 (73.6)	104 (83.2)	0.365
Abnormal PT	0 (0.0)	6 (17.6)	28 (22.4)	0.555
Abnormal INR	1 (33.3)	19 (55.9)	76 (60.8)	0.572
Hypoglycemia	0 (0.0)	0 (0.0)	1 (0.8)	0.862

In a similar study on Argentinian children [13], the average age of children was 6.9 years mostly up to 14 years. Also, in a similar study among Turkish children [14], the mean age was 9.1 years ranging up to 16.5 years. In another study in turkey [15], mean age of infected children was 8.7 years. It seems that age distribution of infection is directly associated with geographical condition; in our region, hepatitis A infection can occur earlier when compared to other regions.

With respect to clinical manifestations, it is also strongly influenced by patient's age. So, clinical course of disease mostly appears in older children and adversely younger children may be asymptomatic. In our survey, almost all children had non-specific symptoms among which, diarrhea was more prevalent in young infants, while older ones suffered from abdominal symptoms. It has been previously pointed that more than 70% of children younger than 6 years old were asymptomatic for hepatitis A infection, while only 20% of older children were asymptomatic [16]. In a study by Çetinkaya and colleagues in Turkey, adolescent patients between 13 and 17 years of age were more commonly symptomatic, having abdominal pain, icterus and dark urine, light-colored stool, myalgia, arthralgia and pruritus [15]. In another study [17], physical examination of infected patients yielded hepatomegaly and splenomegaly, similar to our observation in which about half of the patients manifested with hepatomegaly.

Also, as it was predictable, the most common laboratory abnormalities were related to rising liver enzymes followed by increase of serum bilirubin levels, lowering albumin and abnormal changes in coagulative factors that all markers are naturally produced and regulated in liver. On the other hand, because increase in ALT and AST levels is one of the first signs of hepatocellular inflammation and liver injury [18-20], their changes following hepatitis A infection are well expected. It seems that patients with liver enzyme levels higher than 1000 U/L have worse clinical manifestations [3, 21], and thus require more in-patient closed monitoring as well as longer hospitalization periods.

Conclusion

In conclusion, hepatitis A infection is a common finding among Iranian children that is equally prevalent in boys and girls, while commonly appearing in children aged 7 to 18 years old. Almost all affected children experience non-specific manifestations that commonly include jaundice, repeated vomiting, abdominal pain and fever. The most frequent abnormal changes in laboratory parameters refer to change of liver enzymes, serum bilirubin level, serum albumin and coagulative indices.

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Conflicts of Interest

Authors declare that there is no conflict of interests.

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