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# A Seroepidemiologic Study of Hepatitis A in Seven to Eighteen-Year-Old School Children in Birjand: New Concerns and Opportunities

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## Abstract

**Background:** Hepatitis A is globally spread and is an important public health problem.
**Objectives:** This study aimed at investigating the seroepidemiology of hepatitis A in students aged seven to eighteen years in Birjand, during year 2016.
**Methods:** This study was a descriptive-analytic research, in which 300 school children aged seven to eighteen years in Birjand city were selected through the cluster sampling method. Subsequently, participants and their parents were requested to fill the questionnaire and were referred to the laboratory for blood sampling in order to examine hepatitis A antibody titer. Data were analyzed using SPSS-21 software and the chi-square test.
**Results:** Hepatitis A antibody test was positive for only 111 out of 300 participants (37%). Females (P = 0.009) and teenagers (P = 0.0001) had significantly higher levels of antibody against HAV. There was a significant difference between the presence of hepatitis A antibody, education level of the mothers of the studied individuals (P = 0.042), and the social level and size of the family (P = 0.041). However, no difference was seen regarding fathers' literacy level (P = 0.284).
**Conclusions:** The findings of the study showed that immunity against HAV was reduced during the past years. The reduced level of immunity against HAV along with several major risk factors for HAV infection, such as neighboring with Afghanistan and health hazards of hepatitis A for Iranian pilgrims visiting Karbala-based shrines in Iraq suggest anti-HAV vaccination as an essential priority.

*Keywords:* Seroepidemiology, Hepatitis A, HAV, Schoolchildren, Iran

## 1. Background

Hepatitis A is an acute and usually self-limiting disease with oral-fecal transmission that is caused by hepatitis A virus. Symptoms vary with age; children younger than six are usually asymptomatic, while in older patients, symptoms such as icter may be present (1-3). Hepatitis A is clearly associated with socioeconomic factors as well as access to healthy drinking water and separate sewer system (4, 5). Hepatitis A is widespread across the globe. In 2000, the world health organization estimated that each year, over 1.5 million patients are infected with various distributions in different parts of the world. Regions, such as North America, Western Europe and Australia, are known to have a very low prevalence; North Africa and the Middle East are of a moderate prevalence; and Sub-Saharan Africa is among areas with very high prevalence (6-8). Nevertheless, measures, such as extensive vaccination against the virus, have changed the epidemiology of hepatitis A (9).

Birth in areas with high prevalence of the disease, injective drug abuse, male gender, low education level, large family size, and working in kindergartens and schools are among the main risk factors of HAV infection in Iran (10-13).

Iran has been classified among hyper-endemic areas of hepatitis A (14). Since hepatitis A often shows no clinical symptoms, and a single occurrence causes long-term immunity, vaccination (given the high cost and the impossibility to provide it continuously) is not among priorities of prevention in societies with high prevalence of hepatitis (14). In such societies, the most effective measures for reducing the incidence of hepatitis A infection and possibly of other infectious diseases would be to enhance health and social conditions, e.g. hand hygiene culture, especially

after bowel movements, the use of healthy drinking water, the use of sewage disposal systems, and public health in schools, especially in food centers. However, studies have shown that such measures do not have significant efficacy and that the best way to prevent the spread of infection at the time of its outbreak is vaccination (15).

So far, several studies have been conducted to investigate the seroepidemiology of hepatitis A in Iran, reporting a decreasing trend in terms of the immunity level against hepatitis A among Iranian children and a gradual shift for occurrence of HAV infection in adulthood (16-18). Enquiries into the prevalence of diseases are of great importance in health policy making. The review of the literature indicates that the prevalence of hepatitis A and its risk factors has not yet been fully evaluated in southeastern Iran. Moreover, as schoolchildren are among populations most susceptible to this virus and are often asymptomatic, they are considered as the potential source of its transmission in the community.

## 2. Objectives

The aim of this study was to examine the seroepidemiology of hepatitis A in children of different ages in Birjand, during year 2016.

## 3. Methods

This was a cross-sectional study conducted on children aged 7 to 18 years in Birjand, South Khorasan province of Iran in 2016. Birjand, the largest city in eastern Iran, is the capital of South Khorasan province. It has a cold desert climate with hot summers and cool winters. Precipitation is low and mostly falls in winter and spring. It is bordered to the north with the Razavi Khorasan and Semnan provinces, the south by Sistan and Baluchestan province, the west by Yazd and Kerman provinces, and the east by Afghanistan. The estimated population of Birjand is about 178 000. The city does not have many industries and is surrounded by deserts (19). Based on Sofian et al. (18), the minimum sample size was determined by using the statistical formula of Fisher for calculating sample size ($z^2pq/d^2$) Where; N = Minimum sample size for a statistically significant survey, Z = Normal deviant at the portion of 95% confidence interval = 1.96, P = prevalence value of total anti-HAV of 61% (P = 0.61), q = 1- p (q = 0.39), and d = margin of error acceptable or measure of precision = 0.05 as n=65. In order to increase the precision of the study, the sample size was estimated as 300. Cluster random sampling was employed to select school children.

### 3.1. Participants

The inclusion criteria included being a school child of Birjand in 2016, and willingness to participate in the study. The city was divided to two parts based on economic status of residents, and schools were selected randomly taking an equal portion for each of the two parts. Exclusion criteria included blood transfusion within the past year, receiving intravenous and muscle immunoglobulin within the past year, presence of a known immunodeficiency disease, history of hepatitis A vaccination, being of other nationalities, such as Afghan or Pakistani, and lack of consent to participate in the study. The protocol of the project was approved by the ethics committee of Birjand University of Medical Sciences and written consent was taken from the legal guardians of participants (code: Ir.bums.1394.343).

### 3.2. Assay

For serologic assessment of the incidence of hepatitis A, 5 mL of venous blood was obtained from the anti-cubital area of the body of the participants. Each specimen was centrifuged to isolate the sera. The specimens were then kept in micro-tubes at -20°C until serological tests were performed. An electrochemiluminescence immunoassay (K2-EDTA, Roche, Germany) was used by the Roche-cobas e411 device to assess the presence of total Ig anti-hepatitis A. Information about the participants including age, gender, place of residence, parents' education level, the way of supplying drinking water, and the way of disposing household wastewater were collected using a questionnaire. To complete the questionnaire, both parents and children were incorporated.

### 3.3. Statistical Analysis

Data were analyzed using the SPSS 21 software and both descriptive and inferential statistical tests including independent t-test, Fisher's exact test, analysis of variance (ANOVA), and HSD turkey at the significance level of $P \leq 0.05$.

## 4. Results

Hepatitis A antibody test was positive for only 111 (37%) out of the 300 individuals, who were included in the study (Table 1). None of the studied subjects had received vaccination against HAV. The frequency of positive antibodies in females was significantly higher than in males (40.5% vs. 59.5%, respectively; P = 0.009). Chi-square test results showed significant differences in the distribution of total anti-HAV frequency in terms of age group and mothers' education level (P = 0.001 and P = 0.042, respectively). The

**Table 1.** Demographic Characteristics

| Variable | Frequency (%) |
|---|---|
| **Gender** | |
| Male | 151 (50.3) |
| Female | 149 (49.7) |
| **Age groups, y** | |
| 7 to 8 | 34 (11.3) |
| 9 to 10 | 42 (14) |
| 11 to 12 | 55 (18.3) |
| 13 to 14 | 81 (27) |
| 15 to 16 | 52 (17.3) |
| 17 to 18 | 36 (12) |
| **Mothers' literacy level** | |
| Illiterate | 44 (14.7) |
| Reading and writing | 74 (24.7) |
| Diploma and less | 99 (33) |
| Academic | 83 (27.7) |
| **Fathers' literacy level** | |
| Illiterate | 8 (2.7) |
| Reading and writing | 46 (15.3) |
| Diploma and less | 96 (32) |
| Academic | 150 (50) |
| **Family size, members** | |
| $\leq 4$ | 166 (55.3) |
| 5 or 6 | 124 (41.3) |
| $\geq 7$ | 10 (3.4) |

**Table 2.** Comparison of Frequency Distribution of Total Anti-Hepatitis A Virus Based on Demographic Characteristics[a]

| Variables | Positive anti-HAV ab | Test |
|---|---|---|
| **Gender** | | $X^2 = 6.75$, P = 0.009 |
| Male | 45 (40.5) | |
| Female | 66 (59.5) | |
| **Age group, y** | | $X^2 = 42.36$, P = 0.001 |
| 7 to 8 | 4 (3.6) | |
| 9 to 10 | 4 (3.6) | |
| 11 to 12 | 15 (13.5) | |
| 13 to 14 | 41 (36.9) | |
| 15 to 16 | 26 (23.4) | |
| 17 to 18 | 21 (18.9) | |
| $\geq$ 12 years old | 53 (40.4) | $X^2 = 7.53$, P = 0.0001 |
| Teenager group | 88 (52.1) | |
| **Mother's education** | | $X^2 = 8.18$, P = 0.042 |
| Illiterate | 16 (14.4) | |
| Primary school | 33 (29.7) | |
| Secondary or high school | 26 (23.4) | |
| Tertiary | 36 (32.4) | |
| **Father's education** | | $X^2 = 3.80$, P = 0.284 |
| Illiterate | 5 (4.5) | |
| Primary school | 14 (12.6) | |
| Secondary or high school | 39 (35.1) | |
| Tertiary | 53 (47.7) | |
| **Family size, members** | | $X^2 = 3.80$, P = 0.041 |
| $\leq 4$ | 51 (45.9) | |
| 5 or 6 | 55 (49.5) | |
| $\geq 7$ | 5 (4.5) | |

[a]Values are expressed as No. (%).

frequency of positive HAV cases in individuals with a family of one to four members, five and six, and more than seven members were 45.9%, 49.5%, and 4.5%, respectively (P = 0.041). No relationship was observed between the incidence of HAV and fathers' education (Table 2). All of the enrolled children used refined drinking water, and the system of household wastewater treatment for all the studied subjects was of the kind of sanitary piping. Therefore, no statistical analysis was performed for the two groups in terms of these two issues. Also, most of the participants (98.3%) used vegetables that used healthy watering roles.

## 5. Discussion

This study aimed at investigating the seroepidemiology of hepatitis A among students aged seven to 18 years in Birjand, during year 2016. The findings of the study showed that of the 300 children in the current study, only 37% had positive results for antibody against HAV. The results of the present study indicated that there was a significant declining trend in terms of immunity against HAV in children of Birjand and a gradual shift for occurrence of HAV infection in adulthood. There are great inconsistencies concerning seroepidemiology of HAV between different age groups and within the same age group of different regions, where the HAV prevalence among Iranian children according to the literature ranged from 3% to 90%. However, all of these studies confirmed a common issue, i.e., that there was a significant increase in anti-HAV seroprevalence rate along with age and with decline in immunity level of children. Table 3 shows the seroprevalence of hepatitis A in different parts of Iran.

**Table 3.** The Seroprevalence of Hepatitis A in Children and Adolescents of Different Parts of Iran

| Authors | Year | Location | Population | Sample Size, No. | Prevalence |
|---|---|---|---|---|---|
| **Alian et al.** (16) | 2007 | Sari (North of Iran) | The general population of urban and rural areas | 1034 | 8.9% in 1 to 5 years to 15.8% in 5 to 15 years |
| **Mehr et al.** (17) | 2004 | Tehran (capital of Iran) | Children visited the hospitals | 1018 | 22.3% |
| **Ataei et al.** (20, 21) | 2006 | Isfahan (Center of Iran) | The general population of urban and rural areas (children) | 816 | 10% |
| **Mohebbi et al.** (22) | 2006 - 2007 | Tehran (capital of Iran) | The general population | 551 | 85% in < 30 years |
| **Sofian et al.** (18) | 2009 | Tehran (capital of Iran) | The general population (children) | 1065 | 61.6% |
| **Taghavi Ardakan et al.** (23) | 2012 | Kashan (Center of Iran) | The general population (children) | 666 | 3.9% |
| **Current study** | 2016 | Birjand (Eastern Iran) | The general population (children) | 300 | 37% |

In Saffar et al.'s study on HAV seroprevalence in individuals aged 1 to 30 years in Savadkooh, the data showed that the anti-HAV seroprevalence rate increased significantly with age from 5.7% in the age group of 1 to 2.9 years to 34.8% in adolescents (24). Altogether, studies by Alian et al. (16), Mehr et al. (17), and Sofian et al. (18) in different parts of Iran and on various age groups showed inconsistencies in seroepidemiology of HAV between different age groups and within the same age group of different regions. However, it seems that there is a declining trend in terms of immunity level against hepatitis A in Iranian children and a gradual shift for occurrence of HAV infection in adulthood that urge active immunization via vaccination against this virus (25). Currently, vaccination against HAV is not included in the national immunization program of Iran (26), however, given the high seroconversion rate of HAV among Iranian adolescents, extensive vaccination of children seems reasonable (27).

Given the promoted public health and the increased awareness of people about health issues, a substantial portion of the general population are not infected with HAV. However, it should be noted that the incidence and prevalence of this disease is age-related and the occurrence of HAV infection is influenced by low-to-medium socioeconomic level at early age, and that the prevalence of hepatitis A in each country is very closely related to the health and socioeconomic conditions of that country or region (14). The people's contact rate with the virus, the generation of antibodies in them, age, socioeconomic status, and health conditions of the society are among effective contributors to the occurrence of the disease (28). It is worth mentioning that the geographical situation under study and the economic factors and health conditions of these two regions are different, which can be a reason for this difference. As mentioned earlier, hepatitis A control depends on safe water supply, food safety, improved sanitation, hand washing, and hepatitis A vaccination. In terms of household size, the incidence rate was significantly higher in families with 5 to 6 children. The rate of infection increases with close and prolonged contact with people, who are in the commune period while larger family size increases the likelihood of high risk contacts.

Recently, Mostafavi et al. published the results of the CASPIAN-III Study on prevalence of hepatitis A infection in a sample of 10 to 18-year-old Iranian adolescents living across Iran between 2009 and 2010, reporting a 60% to 70% prevalence rate for hepatitis A in South Khorasan province (29). Children aged seven to 18 years in Birjand had intermediate endemicity for HAV infection; however, its prevalence has decreased by half through the past years (29). These conditions resulted from increased level of hygiene and access to healthy drinking water and separate sewer system. Nonetheless, the reduced level of immunity against HAV as well as several major risk factors for HAV infection (e.g., neighboring Afghanistan and health hazard of hepatitis A for Iranian pilgrims to Karbala-based shrines in Iraq) make anti- HAV vaccination an essential priority (25, 30). In a landmark study by Safiabadi et al., data indicated that the prevalence of hepatitis A virus antibody (IgG) seroprevalence among Afghan and Iraqi populations are more than 95% (31). The best measures to prevent the disease are to vaccinate and to enhance awareness of the transmission and prevention methods. Therefore, using the educational facilities of the country and the mass media for training people is recommended. Of course, it should be noted that vaccination against hepatitis A in endemic countries is not currently recommended due to the established immunity in terms of childhood exposure. According to the results of this study and given the results of previous studies, which suggested the establishment of immunity for childhood exposure in a maximum of 40% of the Iranian population, it seems that vaccination against

hepatitis A could be recommended for Iranian children (32).

### 5.1. Conclusion

Children aged seven to 18 years in Birjand had moderate endemicity for HAV infection; however, its prevalence has decreased remarkably through the past years. These conditions resulted from increased level of hygiene and access to healthy drinking water and separate sewer system. Nonetheless, the reduced level of immunity against HAV along with several major risk factors for HAV infection (long borders with Afghanistan and health hazard of hepatitis A for Iranian pilgrims to Karbala, Iraq) make anti-HAV vaccination an essential priority.

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