RELATIVE SHARE OF ASYMPTOMATIC FORMS OF HEPATITIS A IN PLOVDIV REGION, BULGARIA

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ABSTRACT
OBJECTIVE: To study the relative share of asymptomatic forms of Hepatitis A in family reservoirs of infection with different hygienic conditions.
MATERIALS AND METHODS: Asymptomatic forms were identified by detecting anti-HAV IgM using ELISA. Two types of households: with poor hygiene and with good hygiene, were studied. The study was designed as case-control. A group of Hepatitis A contact children attending day nurseries and kindergartens was also included in the study.
RESULTS: The relative share of asymptomatic forms of HAV infection in poor hygiene households was 58.62%, while in those with good hygiene it was 41.57%. The comparison using Fisher’s exact test yielded OR = 1.99 and 95% CI (P < 0.05). Asymptomatic forms were found in 7.75% of the investigated contacts among children attending day nurseries and kindergartens.
CONCLUSION: Asymptomatic forms of hepatitis A are very common which makes them epidemiologically quite significant as many of the cases remain unrecognized and later become focal points of new cases of the disease. Poor hygiene conditions are likely to cause more asymptomatic forms. The high relative share of asymptomatic forms found in the households supports the need for immunoprophylaxis of the contacts.

Key words: hepatitis A, asymptomatic forms, source of infection

INTRODUCTION
There are no subjective symptoms in HAV asymptomatic cases and laboratory tests (AST, ALT and serum bilirubin) are within normal range.1-3 What is only altered in the infected organism is the readjustment of its immune system to generate permanent immunity.1,2 Asymptomatic forms are identified only by detecting the anti-HAV IgM in the serum of infected individuals.4-6 These forms of HAV infection are of great epidemiological significance because they often remain unrecognized, the contaminated subjects are not isolated and their contacts with other people lead to new cases of the disease.7 There have been reports of epidemiological outbreak of the disease among contacts of first and second degree of an adopted child affected with an symptomatic form of hepatitis A.8 Roohi et al. have also investigated the problem.9 It is quite likely that in cases of HAV with no known previous contact with another patient, there must have been such contact but with a person having asymptomatic infection.10,11

Asymptomatic forms are most common in childhood, accounting for up to 65-85% of all infected patients among children under 5 years of age.5 According to the Prevention and Control of Viral Hepatitis Guidelines valid in Bulgaria now, tests for inapparent forms (anti-HAV IgM) are performed only in contact children in day nurseries and kindergartens in presence of a clinical case after epidemiological assessment.12 Family contacts are not investigated.

AIM
To study and compare the relative share of asymptomatic forms of Hepatitis A in family reservoirs of infection with different hygiene conditions.

MATERIALS AND METHODS
We studied the asymptomatic forms in family reservoirs of two population groups living in different hygiene conditions: group I – poor hygiene conditions; group II – good hygiene conditions. The households of group 1 were from Stolipinovo...
residential district in Plovdiv, Bulgaria, in which the population is predominantly of the gipsy minority.

The district is overpopulated, the households are crowded (most of these up to 4-5 people living in a single room), without sanitized kitchens, bathrooms and toilets. Garbage collection and removal in the district are irregular, often the drainage canals are blocked and waste waters leak on the streets. The population of the district has poor hygiene and health culture. Reservoirs of group II are from the Central district in Plovdiv, where life conditions are good.

Only children under 9 years were included in the study, because inapparent forms are rarer among older children and adults. The study was performed between October 2006 and December 2007. Group I was 116 children, and group II – 89. Serum samples from contacts were obtained between the days 15 and 20 after hospitalization of the clinically manifested cases. They were not taken later, as the incubation period of the disease is 15–45 days, and in that case the infection may be due to contact out of the family. Only cases of anti-HAV IgM positive, clinically negative patients with paraclinical parameters within normal range were defined as asymptomatic. Anti-HAV IgM test was done in the Department of Microbiology, Virology and Immunology at Medical University – Plovdiv using ELISA. Diagnostic devices and tests Dia Sorin were used.

Two hundred and seventy-one children from day nurseries and kindergartens, being in contact with patients with hepatitis A, were also studied. Their serology tests were performed in the virology laboratory of the Regional Health Inspection (RHI) – Plovdiv by ELISA and Pasteur diagnostic tests.

The study design is case-control. The comparison was done using Fisher’s exact test with calculation of OR and 95% CI, using Katz approximation.

Statistic analysis was performed by specialized statistical software SPSS 11.0.

**RESULTS**

In the family reservoirs of patients from group I we studied 116 contact children, with no medical history of hepatitis A (Table 1). They had a mean age of 5 years (ranging from 14 months to 8 years and 10 months); 61 (52.6%) were males. Inapparent forms of hepatitis A was found in 68 (58.62%) of them. Forty-nine of the investigated children from this group were between 1 and 4 years old. Asymptomatic forms were found in 61.22% of them. The rest 67 children were between 5 and 9 years old, 38 (56.72%) of them being positive. Age groups were formed this way, because according to WHO data asymptomatic forms are most common among children under 5 years of age.

In the family reservoirs of patients from group II we investigated 89 contact children, with no medical history of hepatitis A (Table 2). Their mean age was 5 years (range 23 months to 8 years and 4 months); 46 (51.7%) were females. Asymptomatic infection was proven in 37 (41.57%) of them. Inapparent forms of hepatitis A were found in 40.54% of the children between 1-4 years of age, and in 42.31% of those between 5-9 years.

During the period of the study 271 children from day nurseries and kindergartens, who had been in contact with hepatitis A patients, were investigated in the regional Health Inspection Centre. Twenty-one (7.75%) were positive for anti-HAV IgM. The children from this group were not assigned to different age groups because they were all between 3 and 6 years old.

| Table 1. Asymptomatic forms of hepatitis A in reservoirs with poor hygiene conditions |
|-------------------------------|--------|--------|-------|
| **Age** | 1-4 | 5-9 | Total |
| Number of screened | 49 | 67 | 116 |
| of them positive | n | 30 | 38 | 68 |
| proportion ± SE (%) | 61.22 ± 6.96 | 56.72 ± 6.05 | 58.62 ± 4.57 |

| Table 2. Asymptomatic forms of hepatitis A in reservoirs with good hygiene conditions |
|-------------------------------|--------|--------|-------|
| **Age** | 1-4 | 5-9 | Total |
| Number of screened | 37 | 52 | 89 |
| of them positive | n | 15 | 22 | 37 |
| proportion ± SE (%) | 40.54 ± 8.07 | 42.31 ± 6.85 | 41.57 ± 5.22 |
The comparison between the ratio of asymptomatic forms of hepatitis A in the two studied population groups shows significant differences between them (Fig. 1). They concern both different age subgroups and the main groups.

In order to study the impact of poor hygiene conditions of life as a risk factor (and determine its magnitude) on the occurrence of more inapparent forms of HAV in the reservoir of disease, we analyzed the data by the case-control method (Table 3). Our findings suggest that poor hygiene conditions are associated with the presence of higher percentage of inapparent forms of hepatitis A viral infection.

**DISCUSSION**

In approximately 50% of hepatitis A cases, the source of infection was not found, but most probably the patients had been in contact with other people, especially children, with asymptomatic infection. Hepatitis A is a disease which is regarded as mild, especially in children, but presents with severe course in 0.5-1.5% of the patients. In some of those cases the infection is fulminant and the probability for spontaneous recovery is 50%, and the risk of progression to hepatic coma is very high. These figures hold for all age groups. The difference is in the frequency of icteric and asymptomatic forms in children and adults. It is accepted that less than 20-30% of the children under 6 years have jaundice. This implies that hepatitis A is more severe in adults. Children with asymptomatic form are contagious because they excrete the virus with the feces. According to data reported at the 3rd World Congress on Infectious Pediatric Diseases in 2002, during epidemic outbreaks, approximately 30% of children under 5 years have hepatitis A viral infection, proven by the presence of IgM anti-HAV.

Despite the low percentage of icteric forms in children, the risk is significant. During the epidemic outbreak in 1995 in Polynesia four patients (out of 992) developed fulminant hepatitis A, two of whom died; all were between 5 and 12 years old. During the epidemic of hepatitis A in Plovdiv, Bulgaria in 2006, two children (3 and 4 years old) died. Our data prove higher ratio – 51.2% (of investigated 205 children in both groups, positive are 105) of asymptomatic forms in comparison with reports from other authors: 25 – 40%. The asymptomatic forms have much higher frequency in households with poor hygiene conditions. Compared to the frequency in reservoirs with good hygiene conditions, odds ratio is 1.99 (95% CI: 1.14-3.49; P = 0.017). This shows clearly that poor hygiene conditions are associated with greater number of HAV asymptomatic forms.

The significant difference we found between asymptomatic forms in family reservoirs and day nurseries and kindergartens is probably due to daily control measures for prevention of intestinal infections in day nurseries and kindergartens, and the timely discharge of children with symptoms or suspicion of such. In addition, the investigated children are not only from the group of ill children, but also from other groups, with whom the infected had not been in such a close contact, as the case is in family reservoirs.

**Table 3.** Assessment of the risk of occurrence of asymptomatic infection in reservoirs with poor hygiene conditions

<table>
<thead>
<tr>
<th>Exposition</th>
<th>Infection</th>
<th>presence</th>
<th>absence</th>
<th>total</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor hygiene conditions</td>
<td>68</td>
<td>48</td>
<td>116</td>
<td></td>
<td>0.017</td>
</tr>
<tr>
<td>Good hygiene conditions</td>
<td>37</td>
<td>52</td>
<td>89</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OR = 1.99; 95%CI: 1.14 – 3.49
In November 2008 in Riga, an international meeting of European experts, including European Centre for Disease Control (ECDC), was held provoked by the outbreaks of hepatitis A in some countries. In the final discussion it was stated that effective control of hepatitis A epidemics depends also on timely registration of all cases and immunoprophylaxis in all their contacts. Since most of the cases are asymptomatic, they also have to be taken into account.

CONCLUSIONS

We found a high relative share of HAV asymptomatic forms in family reservoirs of infection. It is significantly higher in reservoirs with poor hygiene conditions.

Our results show that the immunoprophylaxis of the contacts in family reservoirs is absolutely necessary, not just recommendable.

Identification of asymptomatic forms of the disease is grounds for the conduction of immunoprophylaxis of the contacts outside the family.

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REFERENCES

ИССЛЕДОВАНИЕ ОТНОСИТЕЛЬНОЙ ДОЛИ БЕССИМПТОМНЫХ ФОРМ ГЕПАТИТА А В ПЛОВДИВСКОМ РЕГИОНЕ БОЛГАРИИ

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РЕЗЮМЕ

Цель: Работа ставит себе целью изучить и сравнить относительную долю бессимптомных форм гепатита А в фамильных очагах заразы с различными гигиеническими условиями.

Материал и методы: Бессимптомные формы определены наличием anti-HAV IgM. Его доказывание проведено с помощью ELISA. Исследование проведено среди двух типов фамильных очагов: 1. С плохими и 2. С хорошими гигиеническими условиями. Дизайн исследования – случай / контрольная группа. Обследована и группа детей, имеющих контакт с гепатитом А и посещающих детские заведения.

Результаты: Относительная доля бессимптомных форм гепатита А вирусной инфекции в фамильных очахах с плохими гигиеническими условиями – 58.62%, а в очагах с хорошими гигиеническими условиями – 41.57%. Результат сравнения - по методу Fisher’s exact test с вычислением OR и 95% CI – 1.99; P < 0.05. Среди детей, посещающих детские заведения, обнаружены бессимптомные формы в 7.75% случаев.

Заключение: Бессимптомные формы гепатита А встречаются часто и имеют большое эпидемиологическое значение, так как большая их часть остается нераскрытой и это приводит к возникновению новых случаев гепатита А. Плохие гигиенические условия обуславливают большое число бессимптомных форм. Высокий процент бессимптомных форм в фамильных очахах подкрепляют необходимость в иммунопрофилактике контактных лиц.