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ORIGINAL ARTICLE

Seroprevalence of hepatitis A virus antibodies (anti-HAV) in adult inhabitants of Wielkopolska region, Poland – the role of simple demographic factors

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Abstract

Introduction and objective: Based on the available epidemiologic data, Poland currently has the features typical for areas of very low endemicity for hepatitis A. The incidence of hepatitis A in the Wielkopolska region in years 2006-2008 was 0.68/100,000 inhabitants or significantly lower. The aim of this cross-sectional analysis was to evaluate the seroprevalence of anti-HAV antibodies in inhabitants of the Wielkopolska region of western Poland regarding some demographic factors.

Material and methods: In addition to testing anti-HAV antibodies, the medical history and demographic data, such as age, gender, place of residence, and level of education of 680 patients and 105 healthy blood donors were analyzed.

Results: Anti-HAV antibodies were observed in 235 cases (29.9%). In univariate regression analysis, the covariates correlated with positive anti-HAV testing were age, female gender and lower level of education. Only 6.2% of young adults were seropositive. Among study participants above the age of 50, anti-HAV antibodies were present in 64-100% of cases. An icteric disease consistent with hepatitis A diagnosis was identified in the histories of 10.2% of seropositive patients.

Conclusions: The risk for contracting disease after exposure to HAV in young (<40 years old) inhabitants of the Wielkopolska region is high. Apart from older individuals, also women and people with a lower level of education are more frequently seropositive. A low level of immunity to HAV should be an indication for vaccination against HAV , especially in selected groups.

Key words

HAV, anti-HAV, seroprevalence, age, gender, education, living place

INTRODUCTION

Hepatitis A virus (HAV) is a member of the distinct genus Hepatovirus within the Picornaviridae family [1]. The characteristics of this virus corresponds to the features of all viruses belonging to this group, i.e. small, non-enveloped, with linear, single-stranded, positive-polarity RNA as a genome, and with capside of icosahedral symmetry [2]. The virus is relatively resistant to many environmental factors and low pH of the stomach, but can be inactivated with typical disinfectants.

The clinical course of HAV infection can vary from asymptomatic forms (most commonly seen in children) or nonspecific flu-like illness, to icteric hepatitis (most cases are seen in the older age groups), and rare but potentially fatal fulminant hepatitis [3]. According to data from Polish National Institute of Hygiene, and from personal experience, there was one death of a patient in 2010. There have been three deaths related with hepatitis A in the last 10 years in Poland) [4, 5, 6].

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Based on the available epidemiologic data, Poland currently has the features typical for areas of very low endemicity for hepatitis A [7, 8, 9]. In the last 10 years, the mean number of reported cases was 254 (from 42 to 738) [8] (Fig. 1). Compared with the past, the present lower incidence of hepatitis A in Poland seems to be particularly related to the improvement of sanitary conditions, socioeconomic status, and higher level of personal hygiene.

Despite the availability of an effective vaccine, the level of vaccinated inhabitants of Poland is too low for its possible influence on an epidemiological situation. Available

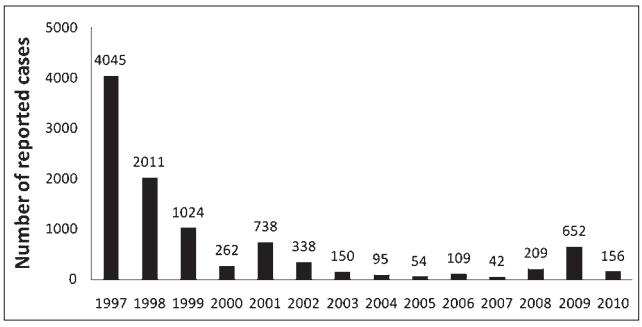

Figure 1. Incidence of hepatitis A in Poland, 1997-2010

epidemiologic data regarding infections with HAV in the Wielkopolska region of western Poland include a number of registered hepatitis A cases and a number of immunizations against this disease in this geographical area. It is one of the largest regions in Poland and in terms of area it is the second largest in the country, and the third most densely populated. The incidence of hepatitis A in this region was as follows: 23 cases in 2006, which corresponds to the incidence of 0.68/100,000 inhabitants, 5 in 2007, an incidence of 0.15/100,000 inhabitants, and 9 in 2008, an incidence of 0.27/100,000 inhabitants. During in the above time period (2006-2008), there were 3,332, 3,087 and 4,548 vaccinations against hepatitis A, respectively [4, 5].

Although the detailed national data from 2009 and 2010 are not yet available, it can be reported that 54 and 29 adult patients, respectively, were hospitalized due to HAV infection in the Poznan Department of Infectious Diseases during these two years.

Objective. The aim of this cross-sectional analysis was to evaluate the seroprevalence of anti-HAV antibodies in inhabitants of the Wielkopolska region, Poland, regarding some demographic factors (age, gender, place of residence, level of education).

MATERIAL AND METHODS

785 persons, aged from 18-87 years (mean 39.2 ± 15.5 years) were included in the presented study. The majority (680/785, i.e. 86.8%) were patients hospitalized or had consulted in the Department of Infectious Diseases at Poznan University of Medical Sciences between 1 January 2009 – 15 October 2010. 105 subjects (13.4%) were healthy blood donors at the Regional Centre For Blood Donation and Therapy of the city of Poznan. The reasons of hospitalization or consultation were: acute and chronic liver diseases, jaundice, acute gastroenteritis, chickenpox, fever of unknown origin, a few cases of botulism, measles and leptospirosis. All patients lived in the Wielkopolska region, western Poland. 453 men (57.7%) and 322 women (42.3%) were tested. 50% of the patients were below the age of 35. Medical histories and demographic factors data, such as age, gender, place of residence, and level of education were analyzed. All patients with a history of jaundice were asked if they had ever been diagnosed with hepatitis A. Patients who were vaccinated against hepatitis A (n=12) and individuals infected with HIV and/or HBV were excluded from the study. Anti-HAV total (IgM and IgG, anti-HAV) antibodies were performed to confirm past HAV infection. Microparticle Enzyme Immunoassay (MEIA, AxSYM HAVAB 2.0, Abbott Laboratories, Wiesbaden, Germany) were used. The results were considered positive if the fluorescence intensity in tested sera in relation to cut-off value were from 0.000-1.000, accordingly to the recommendations of manufacturer. Current or recent HAV infections were excluded from the analyzed group of patients on the basis of clinical history and biochemistry. In every doubtful case, additional serological testing for anti-HAV IgM antibodies (AxSYM HAVAB-M 2.0, Abbott Laboratories, Wiesbaden, Germany) was performed.

Serological testing was performed on serum collected previously for routine diagnostic tests for differential diagnosis or problems requiring consultation, and/or hospitalization in the Department of Infectious Diseases. Written informed consent was obtained for all participants of the study.

The dependence of past HAV infection occurrence on covariates (age, gender, place of residence, education level) was analyzed by logistic regression model. The significance of models were determined by chi-square statistic -2 ($\log(L_0)$-$\log(L_A)$), where L is the maximum likelihood function of, respectively, null and the analyzed model. The significance of particular covariates in the analyzed model was determined by Wald statistics. For significant variables, a unit change odds ratio was calculated. Comparison between two groups was performed by the nonparametric Mann-Whitney test. In the case when data came from the nominal measurement scale, chi-square test of independence was used. All tests were considered significant at $p<0.05$. The calculations were performed by statistical package Statistica 8.0 (StatSoft).

RESULTS

Anti-HAV antibodies were observed in 235 cases; this means that less than one third (29.9%) of all tested persons were seropositive (Tab. 1). The seroprevalence of anti-HAV is higher in older age and it has been proved that this trend is linear in the statistical sense, i.e. differences are statistically significant ($p<0.0001$).

Table 1. Age and frequency of anti-HAV positivity in the analyzed population (n=785)

Age [years]	No. of patients	% of patients with anti-HAV(+)
18-30	305	3.9
31-40	133	11.3
41-50	112	35.7
51-60	169	63.9
61-70	44	86.4
>70	22	100.0

Anti-HAV antibodies were more frequently detected in women than in men (36.5% vs. 25.2%). The difference was statistically significant ($p= 0.00065$). Moreover, the women were older that the men (42.1 ± 16.3 years vs. 37.1 ± 14.6 years, $p=0.00005$) in the studied cohort.

The characteristics of seroprevalence of HAV in the correlation with educational level is shown in Table 2. The patients with a lower level of education were older than patients with higher education (42.3 ± 15.9 years vs. 37.9 ± 15.1 years, $p=0.003$). Men more frequently had a lower level of education than women (39.6% vs. 30.6%, $p=0.02$).

The seroprevalence of anti-HAV was 31.9% in the subgroup of 573 city inhabitants and 24.5% in the subgroup of 212 rural inhabitants ($p=0.04$). There was no statistical

Table 2. Level of education and frequency of anti-HAV positivity (seroprevalence) in analyzed patients (n=592)

Level of education	No. of patients	% of patients with anti-HAV(+)
Elementary school	53	37.7
Technical school	158	37.3
High-school	248	27.8
University/College	133	22.6

difference regarding the gender in above group of patients (p>0.05). Patients living in cities were older (40.3±15.6 years vs. 36.,3±14.8 years, p=0.0009) and had a higher level of education than those living in rural areas (73.5% vs. 60.2%; p=0.0083).

In univariate regression analysis it was shown that covariates correlated with positive anti-HAV were:

– age: a unit change odds ratio for the presence of anti-HAV increased by 1.14-times (95% CI: 1.12-1.16; p <0.0001) with each year of life in this study population, and for patients over the age of 40, antibodies were detected about 3.5 times (OR=3.64; CI: 2.52-5.25) more frequently than in young adults (p <0.0001);
– female gender (OR=1.74; CI: 1.17-2.47; p=0.005);
– lower level of education (OR=1.74; CI: 1.09-2.64; p=0.017).

There was no difference in seroprevalence of anti-HAV regarding the place of residence. A trend towards more frequent seropositivity was observed among city inhabitants (p=0.069).

It was impossible to make a significant multivariate model for dependence of anti-HAV positivity on analyzed covariates.

Among all 785 participants in the presented study, only 24 patients (3.0%) reported an episode of non-surgical jaundice in their medical history. 13/24 cases were finally diagnosed with hepatitis A (based on oral information from the patient or reliable documentation confirming this diagnosis). In 11/24 cases, the diagnosis remained unknown. In all 24 patients with an episode of non-surgical jaundice in the past, anti-HAV antibodies were detected, which means that in at most 10.2% of seropositive inhabitants of the Wielkopolska region of western Poland, overt disease was reported in their history.

DISCUSSION

This analysis provides knowledge about epidemiological factors related to HAV infection in the Wielkopolska region, with information about seroprevalence of anti-HAV and its correlation with selected demographic factors. The problem of anti-HAV seroprevalence in Wielkopolska was described in the study which consisted of only 202 adult persons more than 10 years ago (1996-1997). It was observed that the antibodies were detected in 64-100% of persons, including the youngest patients [10]. Similar analysis undertaken in the same period of time in the Warsaw region (east-central Poland) showed that in patients aged from 16-25, anti-HAV antibodies were detected in 31-38%, between 26-30 years – in 58%, and in fourth decade of life in 71-76%; 90% of the population aged over 40 were seropositive [10].

The results of older study undertaken in young adults in Wielkopolska region contrasted also with data from analysis made in the Lublin region in eastern Poland – from 21.4% seropositivity among persons aged 20-29, to 75.8% in participants over the age of 50 years [11], and among 81 patients hospitalized in the Department of Infectious Diseases in Bialystok, in north-east Poland, because of chronic hepatitis C: anti-HAV positive in 38.5% and 83.6% of patients in the groups aged 18-34 and over 35, respectively, in 1998-1999 [12]. Analysis for the presented study shows that susceptibility to HAV infection among young adult (aged under 40) inhabitants of the Wielkopolska region is common. It is also relatively frequent in the fifth decade of life, but decreases thereafter. This corresponds well with epidemiological data about the current situation regarding hepatitis A in Poland, defined as an area of very low endemicity for HAV infection [7, 8, 9]. It is worth mentioning that in the presented study the seropositivity for anti-HAV antibodies in young adults (aged 18-40) was several times less frequent than values reported from the Warsaw region for 358 patients of similar age (20-39) examined in 2004-2005 (6.2% vs. 35.7%, respectively) [6].

Even if there are only a few current analyses about this issue, based on available data, it can be hypothesize that the frequency of past infection with HAV in young adults may differ significantly according to geographical region; it can be further postulated that these differences depend on socio-economic factors. The role of age in this area is well established, althought the significance of other factors is elusive.

An important limitation to the presented study which had an impact on the assessment for the significance of final results, was the relatively small cohort group tested. It is possible that the lower level of education was correlated with worse adherence to rules of hygiene and more difficult conditions of living in the past, especially in older participants of the analysis, for whom their childhood and adolescence were at the time of high hepatitis A incidence in Poland.

The presence of the female gender on the list of factors associated with past HAV infection probably reflects the fact that the women in the presented study were older than the men. The results obtained confirm that the substantial majority of seropositive individuals experienced a subclinical course of hepatitis A: only about 10% of patients with positive anti-HAV had icteric disease in their history. This suggests an infection in childhood in a large proportion of this group. These data correspond well with epidemiological knowledge about this subject. A low level of immunity (natural or by vaccination) against hepatitis A makes a population susceptible to the occurrence of epidemics in a particular situation [13, 14, 15]. To confirm this contention with an example from the Wielkopolska region, a small outbreak of this disease, observed in the town and district of Gostyn in 2009 can be cited. Among 54 patients hospitalized at that time in the Department of Infectious Diseases in Poznan due to hepatitis A, a significant proportion of them (22/54, i.e. 41%) were inhabitants of that area [16].

The risk of hepatitis A can be significantly reduced by augmentation of vaccination against HAV in a given community [9, 17, 18, 19, 20, 21].

According to the recommendations issued by the Chief Sanitary Inspector for the current year, the National Vaccination Programme 2011, vaccination against hepatitis A in Poland is included into category of recommended procedures, not financed, however, by public expense, particularly for:

– persons travelling to countries of high and intermediate endemicity for hepatitis A;
– workers exposed to sewage;
– food-service establishments and food handlers;
– children at preschool and school age, and adolescents who have not experienced hepatitis A in the past [22].

These recommendations can be completed with some other indications for the mentioned vaccination which are included in the product characteristics provided by the

manufacturer of the vaccine [23]. Among them can be cited (with supporting references): homosexual activity [24, 25], people in direct contact with a hepatitis A case [26], and patients with chronic liver diseases or persons at risk for liver disease [27, 28, 29]. The low number of vaccinated inhabitants of the Wielkopolska region and relatively high cost of the vaccine suggest that realization of this aim will be extremely difficult for physicians. Serological testing for anti-HAV performed in individuals aged 50 and over can lower the total costs of prophylaxis.

CONCLUSIONS

1. In the era of very low endemicity of hepatitis A in Poland, the risk for contracting the disease after exposure to HAV in the young (up to 40 years of age) inhabitants of the Wielkopolska region is high because of common seronegativity (93.8%) for anti-HAV in this age group.
2. Apart from older individuals, also women and people with a lower level of education were more frequently seropositive. Because of the probable frequent coexistence of these factors in this study participants who had experienced HAV infection in the past, the role of gender and level of education in this issue is not clear and require further investigation.
3. An appropriate response to the low level of immunity to HAV should be dissemination of information about the possibility of hepatitis A prevention by vaccination.
4. Pre-vaccination anti-HAV IgG testing in older (aged over 50) inhabitants of the Wielkopolska region may lower the costs of prophylaxis.

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