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PREVALENCE OF ANTI-HAV IGG ANTIBODIES IN THE POPULATION OF THE ŁÓDŹ MACROREGION BY AGE GROUP

Gabriela Henrykowska[1)], Kornelia Kotecka[2)], Aleksandra Jabłkowska[2)], Andrzej Buczyński[1)], Joanna Woźny[2)]

[1)] Epidemiology and Public Health Department, Medical University of Lodz, Poland
[2)] Department of Infectious and the Digestive Tract Diseases, Department of Infectious and Liver Diseases, Medical University of Lodz. Dr. Wł. Bieganski Provincial Specialist Hospital, Poland

ABSTRACT

Over the last several decades, a gradual decrease in the incidence of hepatitis A and an increase in the population of non-immune people, especially in the group of young people have been observed in Poland. The aim of this study was to assess of the presence of specific anti-hepatitis A virus IgG class antibodies (anti-HAV IgG) in relation to age among non-vaccinated hepatitis A patients. There were statistically significantly more patients up to 45 years of age with anti-HAV IgG negative results than those over 45 years of age, and the Fi-square correlation coefficient (Φ2) was 0.263 between the analyzed variables. The data analysis shows that the number of people with specific IgG antibodies against hepatitis A increases with age. The risk of hepatitis A infection in people under 45 is high due to widespread seronegativity in this age group.
Keywords: hepatitis A infection, anty-HAV IgG, seroprevalence.

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INTRODUCTION

According to estimates, cases of hepatitis A virus (HAV) infection affect approximately 1.5 million people per year. These figures may probably be underestimated due to under-reporting of asymptomatic HAV infections [1].

Hepatitis A virus belongs to the family Picornaviridae, genus Hepatovirus. It is a small (27 nm in diameter) non-enveloped virus composed of a single strand of RNA that causes hepatitis A, a generally acute, self-limiting infectious disease. The only reservoir of HAV is humans. The virus is mainly transmitted by the faecal-oral route, as well as through contact with contaminated food and drinking water. Infection can also occur through sexual contact. There is also a potential risk of infection through direct contact with an infected person and blood products [2].

The course of hepatitis A virus infection varies and is largely dependent on age at infection and comorbidities. An asymptomatic course is particularly observed in children under 6 years of age; only about 10% of HAV infections in this patient group present symptoms [3]. In adults, clinical symptoms occur in 76%-97% [4]. The prognosis and course in previously healthy patients is good. The rapidly progressive form (hepatitis fulminans) is observed in 0.1-0.2% of patients, especially over 50 years of age with coexisting chronic liver disease [5]. The mortality rate in this group is 50%. Hepatitis A does not progress to the chronic form. The mortality rate is 0.14-0.2% [6], and post-disease immunity persists for life [7].

The incubation period is 15-50 days (on average 30 days). Between 14 and 21 days before the onset of jaundice, large amounts of virus are excreted from the body. Increased liver enzymes and anti-HAV antibodies in the IgM class are observed [8] Markers of acute hepatitis are present 5-10 days before the onset of symptoms. The presence of antibodies in this class averages 3 months. Thereafter, seroconversion and gradual emergence of antibodies in the IgG class are observed, which persist for life protecting against re-infection [7,9].

A gradual decline in incidence has been observed in Poland over the last few decades, moving from a high risk of infection to one of the lowest incidence rates among European countries [10]. The observed downward trend is likely to have been caused by several concurrent factors such as improved sanitation and hygiene, improved socio-economic conditions, as well as increased food safety and availability of vaccines [11]. These changes have led to a decrease in the incidence of the disease in childhood, in favour of a vulnerable adult population.

Epidemiological data show that as many as 80% of people under 35 years of age are un-immunized, and in the under-40 group only 6.5% have specific antibodies against hepatitis A [12].

AIM

The aim of this study was to assess the presence of specific anti-hepatitis A virus IgG class antibodies (anti-HAV IgG) in relation to age among non-vaccinated hepatitis A patients.

MATERIAL AND METHODS

We analysed the data of 3,121 patients, hospitalised in the period from 1 January 2012 to 31 December 2019 in the infectious diseases wards of the Dr Wł. Biegański Provincial Specialist Hospital in Łódź, who had specific IgG class antibodies against hepatitis A virus (anti-HAV IgG) determined and were not vaccinated against this type of virus. Due to the small number of people, the 90+ group was included in the 80-89 group. For statistical analysis, the newly created group was marked as 80+. The size of the groups in each age range is shown in Figure 1.

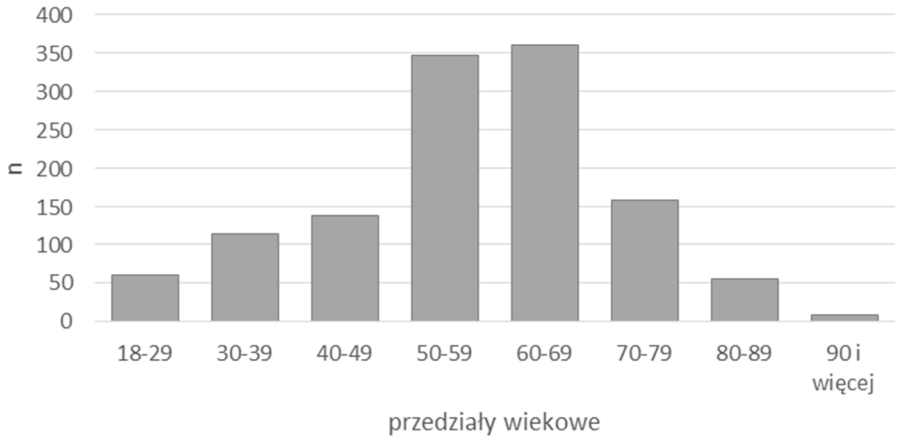

Fig. 1 Age distribution of study population.

The collected data was processed using the Statistica v 13 program and descriptive statistical analysis as well as the Shapiro-Wilk normality test. On the basis of this test, no normal distribution was found in each of the studied groups ($p < 0.001$). Therefore, the Mann-Whitney U test was used for further analysis. In order to determine the relationship between the occurrence of anti-HAV antibodies and the age group, the Fi-square correlation coefficient (Φ^2) was used. The value of the adopted significance level was $p < 0.05$.

RESULTS

In the analysed group, 39.79% of the study population (n=1242) were positive for IgG class specific anti-HAV antibodies. The mean age of the study population was 46.25 years and the median 45 years. Among those with a positive anti-HAV IgG result, the median as well as the mean age were significantly higher than among those with a negative result. The 95% confidence interval (95% CI) values are shown in Table 1.

Tab. 1

Study population broken down by the anti-HAV IgG result.

	n	Mean	SD	Median	min.	max.	95% CI
anti HAV-positive	1242	58,17	14,51	60	18	93	57,36 - 58,98
anti HAV-negative	1879	38,37	12,70	36	18	85	37,79 - 38,94
total population	**3121**	**46,25**	**16,57**	**45**	**18**	**93**	**45,67 46,83**

A statistically significant ($p<0.001$) difference in mean age was observed between the anti-HAV IgG positive and negative groups. For those with IgG antibodies, the mean age was higher than for those with a negative anti-HAV test (58.17 ± 14.50 and 38.37 ± 12.69, respectively). Similarly, significant statistical significance was observed for median age, which was higher among anti-HAV-positive than anti-HAV IgG-negative individuals (Fig. 2).

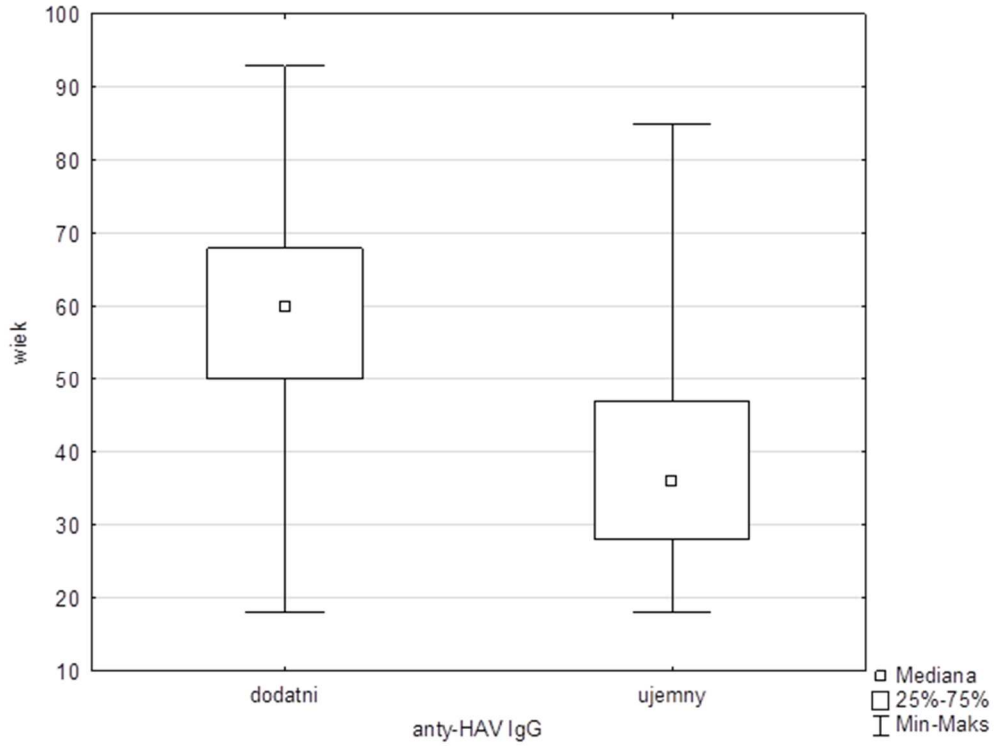

Fig. 2 Age distribution of study population for different anti-HAV IgG test.

In each of the years covered by our analysis (2012-2019), a statistically significant difference ($p<0.0001$) was observed between the age of IgG-positive and IgG-negative anti-HAV test subjects. The results obtained are shown in Fig. 3.

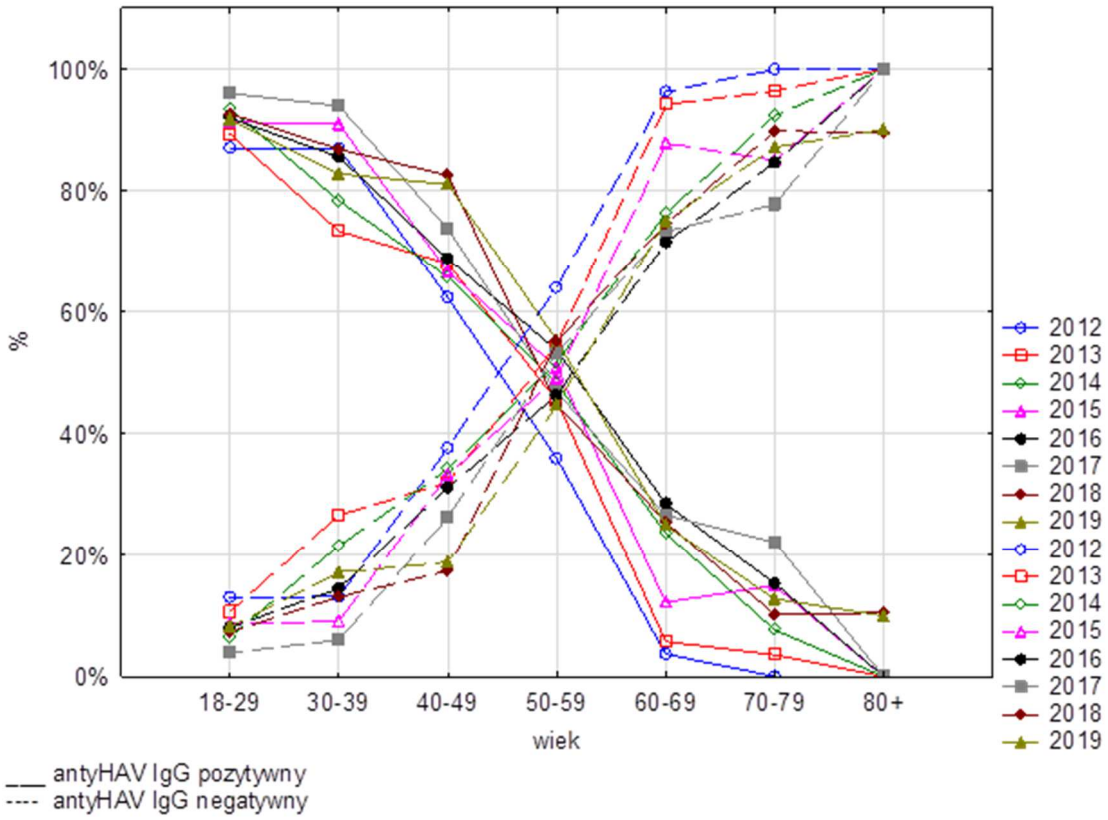

Fig. 3 Prevalence of anti-HAV class IgG antibodies by age group in subsequent years of the study.

A statistically significant correlation was also observed between the different age groups and the result for the entire study population. The positive value of the Spearman's R coefficient in successive years of the study (2012-2019) ranged from 0.66 to 0.58 which proves the high correlation. It indicates that the number of HAV positive cases increases with age in each year of the study.

In further analysis, taking the median age value for the whole group (45 years) as a criterion for dividing the study population, a statistically significant ($p<0.0001$) relationship was observed between the age of the subjects and the anti-HAV IgG result obtained ($\chi^2=819.44$). The value of the Fi-quadrat correlation coefficient (Φ^2) was 0.263 between the variables considered, indicating that the number of people with specific IgG class hepatitis A antibodies increases with age (Fig. 4).

When examining the interaction between the age of the subjects and the presence of specific anti-HAV IgG antibodies, statistically significantly more patients under 45 years of age were observed to be anti-HAV IgG negative than subjects aged 45+ (Fig. 5). In the group over 45 years of age, 65.09% (n=1007) of patients were positive for anti-HAV IgG. In contrast, only 540 patients were negative, representing 17.30% of the total study population. In the group under 45 years of age, only 14.93% of the subjects (n=235) were positive for this test, and 85.07% of this group were negative.

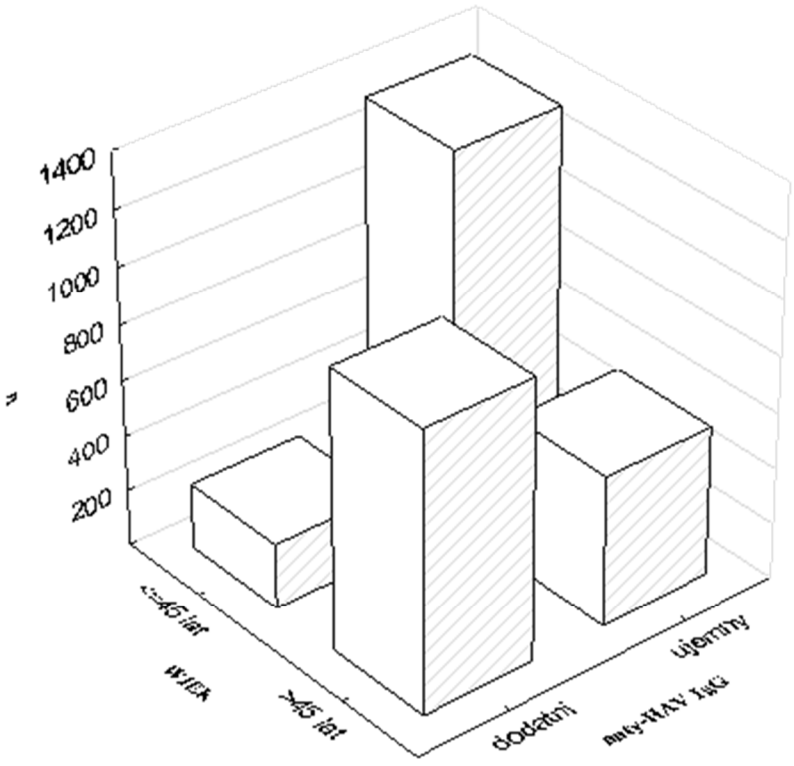

Fig. 4 Correlation between age and anti-HAV IgG test result.

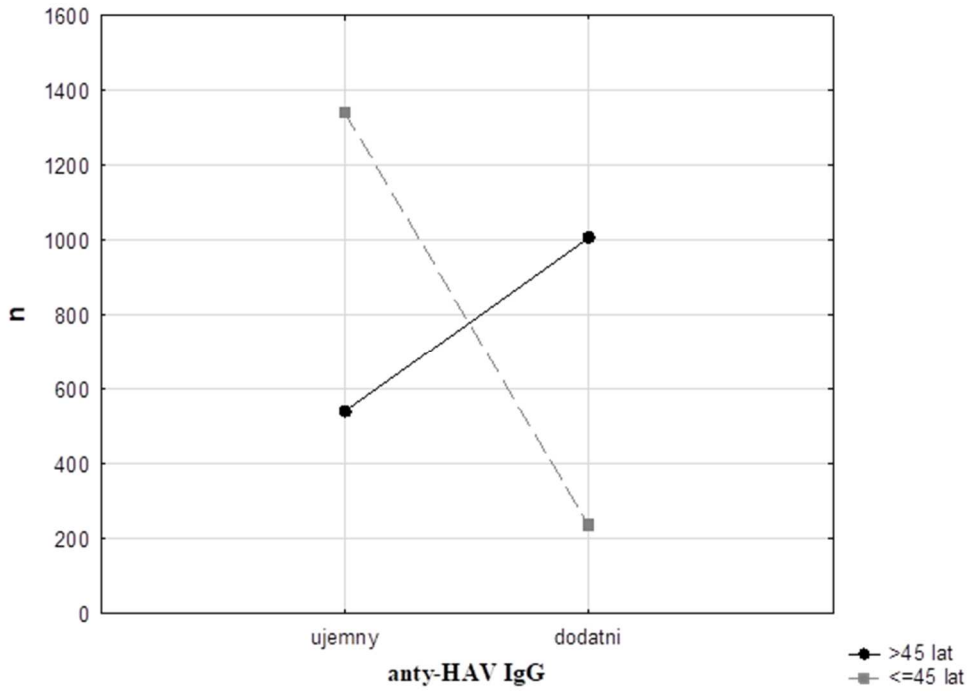

Fig. 5 Presence of specific anti-HAV class IgG antibodies by age.

DISCUSSION

The prevalence of HAV in a population correlates with sanitation, hygiene and socio-economic conditions. HAV endemicity is most commonly classified as high, intermediate and low based on anti-HAV IgG seroprevalence (>50%, 15-50% <15%) [13]. High endemicity is observed in countries with poor/low sanitation and hygiene (mainly in Africa and Asia).High seroprevalence reflects that the majority of the population is resistant to HAV [14].

In developing countries in Asia, Africa or South America, evidence of infection is almost universal. In contrast, the incidence in many European countries, the USA or Canada is low [6,10,15].

A study conducted in Korea showed an overall HAV seroprevalence of 63.8% [74]. In Japan, there was a significant decrease in HAV seroprevalence over 30 years, from 96.9% in 1973 to 12.2% in 2003 [17].

In a seroprevalence study carried out among French soldiers Lagarde et al. found the prevalence of HAV antibodies to be 16.3% [18]. A study of the German population [19] indicates that HAV seroprevalence among adolescents and adults is less than 40% at the age of 30 years.

In our study, we observed that the proportion of immunized persons over 45 years of age was significantly higher compared to the younger part of the population. This may be due to the fact that in the 1970s Poland was among the countries with high HAV endemicity, with an incidence estimated at about 250/100 000 persons [20].

According to a study conducted in the USA, there has been a significant decline in HAV immunity among the adult population between 1988-1994 and 1999-2006 [21]. An increase in hospitalisation rates among HAV-infected individuals has also been demonstrated due to a higher rate of symptomatic infections among the adult population over the past decade [22].

Our own study also revealed a significant decline in HAV immunity in the adult population under 45 years of age.

In children, HAV is usually asymptomatic. Prognosis is usually good and mortality is low (0.1%). Mortality rate increases proportionally with age, up to 2.1% among people aged ≥40 years [66]. Shifting the age group in which HAV incidence is most common towards adults has increased the prevalence of symptomatic disease [23,24]. Data routinely collected for epidemiological surveillance in Poland show that in the years analysed (2012 -2019), of all new cases of hepatitis A, 90-100% required hospitalisation [12].

Our original research shows that 87-96% of people under 29 years of age (depending on the year analysed) do not have specific anti-HAV IgG antibodies.

In a Janaszek-Seydlitz et al. study conducted on a selected population of Warsaw residents, it was shown that anti-HAV antibodies in the IgG class were detected in only 31-38% of patients aged 16-25 years, and 90% of the population over 40 years of age were seropositive [25]. Similarly, a study conducted in the Wielkopolska region showed a higher susceptibility to HAV infection among adults under 40 years of age [26]. In other Polish studies, seropositivity ranged from 21.4 per cent in the age group 20-29 years to 75.8 per cent for those over 50 years of age [27]. A study conducted at the Infectious Diseases Unit in Bialystok, Poland, showed that anti-HAV positivity was observed in 38.5 per cent of patients aged between 18 and 34 and in 83.6 per cent of those aged over 35 [28].

Our own study also showed low seroprevalence among those under 45 years of age. Only 14.93% of the study population was positive for anti-HAV IgG. As many as 85.07% of this group were negative.

The global burden of hepatitis A virus has decreased significantly over the past 20 years [14,20,21]. However, the World Health Organisation (WHO) still defines most of the world's low- and middle-income countries as experiencing high or moderate hepatitis A virus endemicity [1,6]. Most countries in the European Union are classified as areas of low or very low HAV endemicity [10,11]. In such populations (with increasing proportions of susceptible individuals), travel is an important risk factor for infection [24,29,30]. Tourists travelling to countries with high HAV endemicity become infected when consuming contaminated food or drink [11,31,32]. Polish epidemiological data indicate that in 2012-2019, imported cases from countries with high and intermediate HAV endemicity accounted for approximately 31-46% of the total number of hepatitis A cases [12]. The WHO and most EU countries recommend HAV vaccination for travellers visiting countries with intermediate or high endemicity [1,6,10].

Low natural levels of immunity against hepatitis A create an epidemic-prone population. [9,14,16]. The risk of contracting hepatitis A can be significantly reduced by increasing population awareness and encouraging HAV vaccination. This is especially true for people under 45 years of age as well as tourists travelling to highly endemic countries [29,30,33].

CONCLUSIONS

The risk of hepatitis A virus infection in people under 45 years of age is high due to the widespread seronegativity (85.07%) for anti-HAV antibodies in this age group.

People over 45 years of age were mostly seropositive, indicating a history of HAV infection. Almost until the late 1970s, Poland was considered a country with high HAV endemicity.

An appropriate response to the observed low immunization rates among people under 45 years of age should consist in disseminating information about the possibility of preventing hepatitis A through vaccination.
Pre-vaccination testing of specific anti-HAV IgG antibodies in people over 45 years of age may help to reduce the cost of preventive measures.

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dr n. med. Gabriela Henrykowska
Zakład Epidemiologii i Zdrowia Publicznego
Uniwersytet Medyczny w Łodzi
gabriela.henrykowska@umed.lodz.pl