Risk of Anti-Hepatitis A Virus in an Urban Population in Jakarta

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Abstrak

Penelitian sebelumnya mengenai Hepatitis A di Indonesia tidak mengungkapkan prevalensi risiko Hepatitis A pada populasi. Oleh karena itu penelitian ini ditujukan untuk mengetahui prevalensi antibodi terhadap virus Hepatitis A (anti-HAV), dan untuk mengetahui segmen populasi yang mempunyai risiko tinggi, serta faktor risiko yang berguna untuk persiapan program imunisasi. Penelitian dilakukan terhadap 987 subjek berumur 15 tahun ke atas, pada kluster keluarga yang dipilih secara acak pada tahun 1994 di daerah Jakarta Timur. Data yang dikumpulkan antara lain karakteristik subjek (informasi mengenai demografi, sosial ekonomi), faktor risiko terhadap anti-HAV. Di samping itu dilakukan pemeriksaan darah terhadap anti-HAV, SGOT dan SGPT. Hasil tes anti-HAV menunjukkan 87% positif, dan terdapat kenaikan risiko menurut umur, dan mencapai puncak kenaikan risiko sebanyak 18.8 kali lipat (95% CI: 8.0-44.2) di antara yang berumur 51 tahun atau lebih dibandingkan dengan populasi pembanding yang berumur 15-19 tahun. Anti-HAV yang terjadi secara alamiah sangat berkaitan dengan status sosial ekonomi yang rendah. Dibandingkan dengan yang bertaraf sosial ekonomi tinggi, yang bertaraf sosial-ekonomi rendah mempunyai risiko 4.9 kali lipat (95% CI: 2.5-9.4). Risiko anti-HAV positif berkurang jika telah mendapatkan imunisasi Hepatitis B, tetapi sebaliknya kepernahan mengalami sakit kuning meningkatkan risiko terhadap anti-HAV. Sasaran imunisasi untuk melindungi infeksi HAV ditujukan golongan dewasa muda terutama dengan taraf sosial ekonomi tinggi yang kiranya kurang mendapatkan imunitas secara alamiah dan yang akan sangat rentan terhadap infeksi HAV bila beranjak dewasa..

Abstract

In Indonesia, prior studies to identify risk factors for hepatitis A have not provided prevalence estimates in the general population. This study was conducted to measure the prevalence of antibody to hepatitis A virus (anti-HAV), and to identify high risk populations and risk factors in preparation for an immunization program. Using randomly selected households in Jakarta, 987 adults and adolescents aged 15 and older were interviewed in 1994 to ascertain demographic information, socioeconomic status and risk factors for anti-HAV. Blood samples were taken for anti-HAV, SGOT and SGPT. Eighty seven percent of the participants were positive for anti-HAV. Risk increased with age, reaching an 18.8-fold risk (95% CI 8.0-44.2) among those aged 51 years and over, compared to the reference group aged 15-20 years. Anti-HAV was strongly associated with low socioeconomic status (odds ratio 4.9, 95% CI 2.5-9.4). Immunization against hepatitis B was associated with reduced risk of anti-HAV, and a history of jaundice increased the risk of anti-HAV. Immunization against HAV should be targeted to adolescents and young adults, particularly those in higher socioeconomic groups, who are least likely to have natural immunity and who are most susceptible to HAV infection in adulthood.

Keywords: *Hepatitis A, Immunity, Epidemiology, Risk*

INTRODUCTION

Hepatitis A is endemic in Indonesia as well as in other South Asian countries [1,2,3] and it is established that risk is related to environmental sanitation. Although hepatitis A virus (HAV) infection is rarely fatal, it is a serious medical problem and is associated with substantial costs. Worldwide, over 1.4 million cases occur annually, with roughly half of these in Asia, and with costs estimated at $1-3 billion per year.[4] Symptomatic as well as asymptomatic hepatitis A infection can induce the production of long lasting IgG antibodies to hepatitis A virus (anti-HAV).[5]

Although improvements in sanitation have reduced the incidence of hepatitis A in many countries, sanitation programs are costly and take years to implement, leaving a large segment of the population susceptible to infection.[6] Inactivated virus vaccines, which have recently become available, promise to play an increasing role in the prevention of hepatitis A. However,

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since immunization is costly, the identification of groups at high risk of infection is an essential element in targeting immunization programs. Prior studies of hepatitis A prevalence in Indonesia have focused on special groups such as blood donors, students, hospital employees, and patients [1,7] but they are of limited value in identifying high risk groups in the general population. Therefore, we conducted a community-based study on anti-HAV to identify high risk populations as an initial step in planning an immunization program. Understanding of the epidemiology of hepatitis A facilitates decisions on the proper use of vaccines.

METHODS

This study was conducted during January to June 1994 in an urban subdistrict of Jakarta, Indonesia which contained 34,666 people in 7,017 households. Three hundred and forty households were selected randomly and all family members aged 15 or older were asked to participate. A total of 1,150 subjects from these households were eligible to participate in the study. Specially trained nurse-midwives visited the homes of the eligible subjects to evaluate socioeconomic conditions and to invite the subjects to visit a local, participating hospital for this study. The nurse-midwives then conducted structured interviews of the subjects at the participating hospital regarding demographic characteristics and risk factors for anti-HAV, such as gender, age, education, social status, medical history related to hepatitis disorders, and history of hepatitis B immunization. Blood samples for anti-HAV, SGOT, and SGPT were taken.

SGOT and SGPT laboratory tests were carried out using laboratory kit tests from Boehringer Mannheim GMBH and tests for anti-HAV were carried out by ELISA (enzyme linked immunosorbent assay) tests, using a commercially available kit (Abbott Laboratories, North Chicago, Illinois). All sera were collected and kept at -20 degrees Celsius prior to the assessment at *Laboratoria Hepatika Mataram,* East Indonesia.

Factors under study included education level (high = study at college/university or more; middle = study at junior or senior high school; low = illiterate, capable of reading only, or study not beyond primary school), gender (female/male), ethanol drinking habits (yes/no), smoking cigarettes (yes/no), sport habits (yes/no), history of transfusion (ever/never), history of hepatitis B vaccination (ever/never), history of jaundice (ever/never), family history of jaundice (ever/never), SGOT level (abnormal = 38 IU/dl for male and = 32 IU/dl for female), SGPT level (abnormal = 42 IU/dl for male and = 32 IU/dl for female), socioeconomic status (high/middle/low), and age (15-20, 21-30, 31-40, 41-50, 51 and over). Determination of socioeconomic status was based on the housing condition, whether transportation was owned, ownership of housing appliances, and whether the house had electricity.

Logistic regression was used to estimate odds ratios for each risk factor in relation to anti-HAV status and to simultaneously control for confounding by other factors. For consistency of presentation, a group of confounders consisting of gender, cigarette smoking, drinking habit, sport habit, history of blood transfusion and/or education level, social status and age group are included in all the models presented. Odds ratios were estimated by the method of maximum likelihood. The 95% confidence intervals (CI) were based on the standard error of coefficient estimates.[8]

This study was approved by the Ethics Committee of the Department of Internal Medicine of the University of Indonesia Faculty of Medicine.

RESULTS

One thousand and twenty out of 1,150 invited subjects (89%) participated in this study. We excluded 33 subjects due to incomplete and/or conflicting data, leaving a total of 987 subjects. Eight hundred and sixty one subjects were positive for anti-HAV and 126 were negative, giving an overall prevalence of 87%. Of the 987 participants, 20.8% (205/987) had a high education level. Anti-HAV positive and negative subjects were similarly distributed with respect to gender, drinking habit, cigarette smoking habit, sport habits and history of blood transfusion (Table 1).

Immunization toward hepatitis B was associated with reduced risk of anti-HAV (adjusted OR = 0.42, 95% CI: 0.23 to 0.75). As expected, a history of jaundice was associated with increased risk of anti-HAV (adjusted OR = 5.32, 95% CI: 1.28 to 22.08). In contrast, a family history of jaundice was reported by only 119 subjects (12%) and was not associated with anti-HAV (adjusted OR = 0.84, 95% CI: 0.48 to 1.45). This may reflect substantial under-reporting of jaundice in family members. Abnormalities of SGOT and SGPT were not statistically significantly associated with anti-HAV (for SGOT, adjusted OR = 1.77, 95% CI: 0.94 to 3.31; for SGPT, adjusted OR = 5.62, 95% CI: 0.71 to 39.16) as shown in Table 2.

Table 1. Demographic factors associated with antibodies to hepatitis A virus (anti-HAV)

	Anti-HAV status			
	Positive (n=861)		Negative (n=126)	
	n	%	n	%
Sex				
Male	396	46.0	62	49.2
Female	465	54.0	64	50.8
Education				
High	173	20.1	32	25.4
Middle	471	54.7	75	59.5
Low	217	25.2	19	15.1
Drinking habits				
No	813	94.4	122	96.8
Yes	48	5.6	4	3.2
Cigarette smoking				
No	638	74.1	101	80.2
Yes	223	25.9	25	19.8
Sport habits				
No	379	44.0	48	38.1
Yes	482	56.0	78	61.9
History of transfusion				
Never	799	92.8	119	94.4
Ever	62	7.2	2	5.6

Table 2. Hepatitis conditions associated with antibodies to hepatitis A virus (anti-HAV)

	Anti-HAV status					
	Positive (n=861)		Negative (n=126)		OR*	95% CI
	n	%	n	%		
Hepatitis B vaccination						
Never	811	94.2	108	85.7	1.00	(reference)
Ever	50	5.8	18	14.3	0.42	0.23 - 0.75
Ever had jaundice						
Never	789	91.6	123	97.6	1.00	(reference)
Ever	65	7.5	2	1.6	5.32	1.28 - 22.08
Unknown	7	0.8	1	0.8	1.07	0.13 - 8.85
History of family *jaundice*						
No	705	81.9	102	81.0	1.00	(reference)
Yes	101	11.7	18	14.3	0.84	0.48 - 1.45
Unknown	55	6.4	6	4.8	1.24	0.52 - 2.98
SGOT						
Normal	715	83.0	114	90.5	1.00	(reference)
Abnormal	146	17.0	12	9.5	1.77	0.94 - 3.31
SGPT						
Normal	828	96.2	125	99.2	1.00	(reference)
Abnormal	33	3.8	1	0.8	5.62	0.71 - 39.16

* Odds ratio adjusted for gender, smoking habit, drinking habit, sport habits, history of transfusion and education group.

The risk of anti-HAV was inconsistently related to education level, with highly educated subjects having the lowest risk. In comparison, those subjects in the middle education group had a risk of 1.81 (95% CI 1.06-3.20) and those in the lowest education group had a risk of 1.24 (95% CI 0.59-2.61).

The risk of anti-HAV was strongly associated with lower socioeconomic status (Table 3). Compared to the high socioeconomic group, the low socioeconomic group had a 4.9-fold risk of having anti-HAV (adjusted OR = 4.86, 95% CI: 2.53 to 9.37). The prevalence of anti-HAV increased consistently with age, from 70% (106/151) among the 15-20 year age group to 95% (228/238) among subjects 51 years and older. Compared to the reference group (ages 15-20 years) risk increased in a stepwise manner with age, reaching a 18.8-fold risk among those aged 51 years and over (adjusted OR = 18.82, 95% CI: 8.02 to 44.20) as shown in Table 3. Although the age-specific prevalence rates are more intuitively attractive, the odds ratios from the logistic regression models are more accurate, as they reflect the adjustments made for the simultaneous effects of all risk factors (including gender, education, and socioeconomic status).

DISCUSSION

Five patterns of infection with hepatitis A virus are recognized in international studies of age-specific sero-prevalence.[4] In the first pattern, seen in the poorest countries, infection early in life leads mainly to subclinical disease and more than 90% of children are infected by age 5 years. A second pattern is seen in countries with slightly better economic conditions, in which fewer children are infected by age 5, but 90% are infected by age 10 years. A third pattern, occurring in countries with moderate endemicity, is characterized by lower prevalence in young children, but rising prevalence with age to reach 90% in early adulthood. Our data indicate that the Jakarta population fits this pattern (Table 3). The fourth pattern, which occurs in developed countries such as the United States, is characterized by prevalence which reaches 10% by age 15 years and slowly rises to 70% in late adulthood. In the fifth pattern, seen in Scandinavia,

Table 3. Socioeconomic status and age relationship with antibodies to hepatitis A virus (anti-HAV)

	Anti-HAV status					
	Positive (n=861)		Negative (n=126)		OR*	95% CI
	n	%	n	%		
Education						
High	173	20.1	32	25.4	1.00	(reference)
Middle	471	54.7	75	59.5	1.81	1.06 - 3.10
Low	217	25.2	19	15.1	1.24	0.59 - 2.61
Socioeconomic status						
High	163	18.9	45	35.7	1.00	(reference)
Middle	398	46.2	62	49.2	2.16	1.36 - 3.46
Low	300	34.8	19	15.1	4.86	2.53 - 9.37
Age (years)						
15-20	106	12.3	45	35.7	1.00	(reference)
21-30	204	23.7	54	42.9	1.95	1.17 - 3.25
31-40	155	18.0	9	7.1	9.58	4.19 - 21.91
41-50	168	19.5	10	7.9	10.43	4.67 - 23.24
51 and over	228	26.5	8	6.3	18.82	8.02 - 44.20

* Odds ratio for **education** adjusted for gender, smoking habit, drinking habit, sport habits, history of transfusion, **socioeconomic status** and **age group.**
Odds ratio for **socioeconomic status** adjusted for gender, smoking habit, drinking habit, sport habits, history of transfusion, **education group** and **age group.**
Odds ratio for **age group** adjusted for gender, smoking habit, drinking habit, sport habits, history of transfusion, **education group,** and **socioeconomic status.**

prevalence is negligible except among older adults who were infected decades earlier.

Hepatitis A infection early in life is most frequently subclinical, while infection in adulthood more commonly results in clinical illness with substantially greater morbidity and occasional fatalities.[4] Thus, as natural immunity developed in early childhood becomes less prevalent, the impact of infection later in life increases. This paradox points to the pressing need for immunization programs in developing countries, especially among sectors of the population who are at high risk of infection during adulthood.

The dramatic declines in the prevalence of anti-HAV that have been observed recently in Taiwan, Thailand and Singapore[2,9] have been attributed to general improvements in hygienic conditions, water quality, and standards of living, which accompany industrialization. Thus, it is likely that the recent, dramatic economic growth in Indonesia will be reflected in falling seroprevalence of anti-HAV over the next decade.

Passive immune prophylaxis with immune globulin has been used effectively to prevent Hepatitis A, but repeated injections are necessary to maintain immunity among persons who live in areas hyperendemic for HAV infection. Unfortunately, patient compliance is usually poor, resulting in high rates of infection.[10] Inactivated and live attenuated hepatitis A vaccines are effective[11,12] and are endorsed by the World Health Organization Hepatitis Program as the most immediately effective measure for viral hepatitis control.[13] However, in order to maximize the benefit of immunization programs, it is necessary to identify the groups at high risk of HAV infection through epidemiological studies.

Our data indicate that HAV vaccination should be targeted to adolescents and young adults (rather than older adults), particularly those in the higher socioeconomic groups. Because the prevalence of anti-HAV is extremely high (94%) in the lowest socioeconomic group, the vast majority of vaccinations in this group will be of no benefit, whereas in the highest socioeconomic group, in which the prevalence of anti HAV is lower (78%), vaccination will be of greater benefit. However, given the universally high risk of anti-HAV in the urban Jakarta population, substantial benefits may derive from a broad immunization program across all socioeconomic groups and educational strata. The 70% prevalence of anti-HAV that we observed among adolescents aged 15-20 indicates that the majority of the population has already been infected with hepatitis A by this age and that immunization of younger adolescents will also be beneficial. The prevalence of anti-HAV in Jakarta children is not well characterized, although recent studies indicates that among children less than 5 years old, the prevalence of anti-HAV is estimated to be between 26%[1] and 36% *(Unpublished data. Sulaiman HA, 1993).* Further characterization of the Jakarta pediatric population is necessary to maximize the benefits of immunization against hepatitis A.

Recent evidence indicates that sero-conversion after vaccination is associated with acquisition of immune memory. The immune memory after vaccination provokes a rapid anamnestic response that is believed to produce a very long-lasting protection from clinical hepatitis A.[14] It is possible that this vaccine immune memory in the presence of high exposure rates among the population may reduce the dosage of HAV vaccine and the cost of vaccination. A study to confirm this possibility should be done in highly endemic areas such as Indonesia.

There are several limitations that must be considered in the interpretation of our findings. First, this study was conducted in an urban population with high educational and socioeconomic status relative to rural areas of Indonesia. Thus, our results may underestimate the prevalence of anti-HAV in rural populations. In addition, our population was limited to subjects age 15 and over and the results for younger children are not known. Our study had a number of methodological strengths, including large size and a population-based design which insure that the results are applicable to the general urban population of Jakarta (currently estimated at 12 million people). In addition, the population we studied had no access to HAV immunization, insuring that our results are unaffected by this intervention. Opportunities to study populations with natural immunity will become uncommon in the near future as the use of HAV vaccines increase. Our participation rate was quite high (89%), making it unlikely that selection bias has played any substantial role in our findings. It is likely our estimates of the prevalence of anti-HAV in this population are reliable and can provide a firm foundation for the planning and implementation of a hepatitis A immunization program.

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