

Age, hepatitis B infection and risk of anti hepatitis B surface antigen

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Abstrak

Dalam makalah ini, yang merupakan sebagian hasil survei komunitas mengenai hepatitis di Jakarta, diungkapkan tentang prevalensi dan faktor risiko yang berkaitan dengan anti hepatitis B surface antigen (anti-HBs). Sampel terdiri dari 995 orang yang berumur 15 tahun keatas. Faktor risiko diidentifikasi dengan mempergunakan kuesioner, dan wawancara dilakukan di rumah subjek. Serum dianalisis terhadap anti-HBs, hepatitis B surface antigen (HBsAg), aspartate aminotransferase (AST), dan alanine aminotransferase (ALT). Hasil penelitian menunjukkan bahwa populasi terdiri dari penduduk yang relatif berpendidikan lebih tinggi. Seroprevalens anti-HBs positif adalah 17,5% (174/995), dan HBsAg positif sebesar 4,1% (41/995). HBsAg positif memperkecil risiko anti-HBs positif (rasio odds suaian = $OR = 0,24$, 95% $CI: 0,06-1,00$, $p=0,051$). Dibandingkan dengan golongan 15-19 tahun, terdapat kecenderungan positif yang bermakna bahwa golongan umur yang lebih tua berisiko lebih tinggi mengidap positif anti-HBs ($p=0,004$), dan mencapai puncaknya pada golongan umur 30-39 dan 40-49 tahun (masing-masing OR suaian = 1,86; 95% $CI: 1,01-3,42$, dan OR suaian = 2,19; 95% $CI: 1,21-3,69$). Kemudian terdapat penurunan risiko di antara penduduk yang lebih tua. Dapat disimpulkan bahwa seroprevalens anti-HBs moderat pada penduduk yang relatif berpendidikan tinggi. Status HBsAg positif memperkecil risiko anti-HBs positif, dan orang yang berumur lebih tua mempunyai kecenderungan berisiko anti-HBs positif.

Abstract

As part of a community-based hepatitis survey in Jakarta, this paper measures the prevalence of anti hepatitis B surface antigen (anti-HBs), and identifies the related risk markers. Sample consisted of 995 people aged 15 years and above. Risk markers were identified by questionnaires and home visits, and serum was analyzed for anti-HBs, hepatitis B surface antigen (HBsAg), aspartate aminotransferase (AST), and alanine aminotransferase (ALT). In a relatively higher educated population, the seroprevalence of anti-HBs positive was 17.5% (174/995), and HBsAg positive was 4.1% (41/995). A positive of HBsAg reduced the risk of positive anti-HBs (adjusted odds ratio= $OR=0.24$, 95% $CI: 0.06-1.00$; $p=0.051$). Compared to 15-19 years age group, there was a significant positive trend that older age groups had increased risk of having anti-HBs positive ($p=0.004$), and reach its peak among aged 30-39 years and 40-49 (adjusted $OR=1.86$; 95% $CI: 1.01-3.42$, and adjusted $OR=2.19$; 95% $CI: 1.21-3.69$ respectively). Afterward the risk was decreasing among elderly persons. In conclusion, the seroprevalence in a relatively well educated population of anti-HBs was moderate. A positive status of HBsAg was lowering the risk of anti-HBs positive, and the older age had a trend of higher risk of having anti-HBs positive.

Keywords: age, hepatitis B, risk of anti hepatitis B surface antigen

INTRODUCTION

In southeast Asia including Indonesia hepatitis B infection are still endemic.¹ There were several serological methods to detect hepatitis B infection, including measuring the prevalence of serum hepatitis B antigen (HBsAg), antibody to hepatitis B surface antigen (anti HBs), antibody to hepatitis B core antigen (anti HBc), and hepatitis B virus desoxyribonucleic acid (HBvDNA). The present of anti-HBs indicates recovery of acute hepatitis B or immunization.

Three antigen-antibody systems have been identified for hepatitis B virus (HBV): HBsAg and anti-HBs,

core antigen and antibody (HBcAg and anti-HBc), and hepatitis B virus e antigen and hepatitis B virus e antibody (HBeAg and anti-HBe).^{1,2} Serological evidence of previous hepatitis infection varies depend on several factors, especially on age and socioeconomic class.¹

Most previous epidemiological studies of anti-HBs markers have focused on special groups such as hospital-based patients, hemophilia patients, and hospital workers, blood donors. Prior studies in high risk groups in southeast Asia suggest that the risk markers for hepatitis B may differ from those seen in Europe and in the United States.^{1,3} Epidemiological studies on hospital-based or special groups not really represent the general population.

Even though the protective immunity follows hepatitis B infection if anti-HBs develops and HBsAg is negative, but to identify this data needs a cohort study. In order to conduct a mass vaccination strategy, therefore based on a community-base study it is beneficially to study some risk markers for anti-HBs in the general population and to define the roles of age and HBsAg as risk markers of anti-HBs.

METHODS

This analysis was a part of the study which was conducted from January to June 1994 in an urban sub-district of eastern part of Jakarta, Indonesia. The subdistrict consisted of 34666 people in 7017 households. In this study, it was selected 340 households randomly. All the household members aged 15 and more were asked to participate. A total of 1150 subjects from these households were eligible to participate in the study. Specially trained nurse-midwives visited the houses of the eligible subjects to evaluate their socioeconomic status, and to invite the subjects to visit a local participating hospital for this study. The nurse-midwives then interviewed the subjects using structured questionnaire at the participating hospital regarding demographic characteristics and risk markers for anti-HBs.

Blood samples for HBsAg, anti-HBs, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were taken.

Laboratory markers under study included anti-HBs, HBsAg, AST and ALT levels. AST and ALT laboratory tests were carried out using laboratory kit tests from Boehringer Mannheim GMBH (normal AST level is less than 38 IU/dl for male, and less than 32 IU/dl for female; normal ALT level is less than 42 IU/dl for male, and less than 32 IU/dl for female).

Tests for anti-HBs and HBsAg were done using reverse passive hemagglutination (PHA) and passive hemagglutination (RPHA) consecutively in Laboratoria Hepatika Mataram, Nusa Tenggara Barat Indonesia. All sera were collected and kept at -20 degrees Celsius prior to the assessment.

The characteristics of subjects included gender, age, education, socioeconomic status, ethnicity, family size, alcohol use. The medical risk markers including history of: jaundice, family jaundice, transfusion, operation, hepatitis B vaccination, normality status of AST, ALT, and HBsAg.

For this analysis based on logistic regression, for each subgroup of risk markers, the reference subgroups were the subgroup which had less or least likely risk of anti-HBs and coded 0. The higher risk subgroup were coded 1 etc.⁴

Age was divided into subgroup of: 15-19 years; 20-29 years; 30-39 years; 40-49 years; 50-59 years; and 60-87 years. Level of education (high = study at college/university or higher level; middle = study at junior or senior high school; low = illiterate, capable of reading only, or study not beyond primary school). Socioeconomic status (high/middle/low) was determined by the evaluation of the nurse-midwife, based on the housing condition, ownership of transportation devices, ownership of housing appliances, and the availability of electricity. Ethnic group (Malayan/Chinese). Family size (1-2 persons/3-4 person/5 persons and over). Current alcohol use (no/yes), history of surgical operations (never/ever). History of jaundice (never/ever), family history of jaundice (never/ever/unknown). History of hepatitis B vaccination (never/ever). History of transfusion (never/ever). History of operation (ever/never).

Logistic regression analysis was used to control the confounding effects of other characteristics and exposures on the relationship to anti-HBs.⁵ Any variable whose univariate test has a *p* value less than 0.25 will be considered as a candidate for the multivariate model along with all variable known biologic importance Characteristics that fulfilled this definition as confounder are included in the models presented.^{4,5} Odds ratios were estimated by the method of maximum likelihood, and their 95% confidence intervals (CI) were based on the standard error of coefficient estimates using Egret software.⁶

This study was approved by the Ethics Committee of the Department of Internal Medicine Faculty of Medicine University of Indonesia. Informed consent was obtained from participants in this study.

RESULTS

A number of 1020 respondents out of 1150 invited subjects (89%) participated in this study. We excluded 25 out of 1020 subjects (2.5%) due to incomplete and/or conflicting data, leaving a total of 995 subjects.

The excluded 25 subjects consisted of 22 who had anti-HBs negative and 3 anti-HBs positive; 24 HBsAg negative and 1 with HBsAg positive. By age group: 1

person belongs to age group of 15-19 years; 5 persons aged 20-29 years; 6 persons aged 30-49 years; 7 persons aged 40-49 years; 3 persons aged 50-59 years; and 5 persons aged 60-87 years. By gender: 13 male and 12 female. By history of jaundice: 22 persons never had jaundice, 3 persons who ever had jaundice. By history of family jaundice: 22 never had, 1 ever had, and 2 unknown. By socioeconomic status the excluded subjects were as follows: 4 belonged to high-level socioeconomic status, 5 middle-level socioeconomic status, and 16 low-level socioeconomic status.

The excluded subjects in term of HBs status, age groups, history of jaundice and history of family jaundice, gender, and socioeconomic status, were not significantly different with the 995 subjects which included in this analysis.

The overall seroprevalence of anti-HBs was 17.5% (174/995).

The youngest subject was 15 years old which follow the criteria of inclusion for this community-based study, and the eldest subject was 87 years old. The biggest number percentage of the subjects came from the middle education level (54.7% = 544/995), followed by high education level of 21.3% (212/995), and with education low of 23.6% (235/995).

The high level of socioeconomic status of the subjects was 24.3% (242/995), and the middle class was 20.6% (205/995), however the largest number come from the low socioeconomic status of 55.1% (548/995).

The univariate analysis results showed that there was no statistical significant relationship in term of gender, education level, socioeconomic status, ethnicity, family size and alcohol use to anti-HBs status (Table 1).

It was also noted from the univariate analysis that there was no statistical significance relationship to anti-HBs status in term of history of: jaundice, family jaundice, transfusion, operation, hepatitis B vaccination, and it also for the normality status of AST and ALT. However HBsAg status reduced the risk a positive anti-HBs by 0.23 times (OR=0.23, 95% CI: 0.06-0.98).

We assumed there were no acute hepatitis cases found in our study because the maximum range of AST and ALT among our subjects was less than 2.5 times the normal limits. The range of AST in our study was 11 to 92 U/l, while ALT ranged from 9 to 87 U/l. (Table 2).

Forty one subjects were tested positive for HBsAg and 954 were negative, giving an overall prevalence of positive HBsAg 4.1%. Those who ever had hepatitis B immunization was 49 persons out of 995 subjects or 4.9%. The univariate analysis showed that a positive result of HBsAg test decreased the risk of positive anti-HBs status.

Our data showed that the other medical risk markers (ever had jaundice, family history of jaundice, history of transfusion, history of operation, hepatitis B vaccination, and abnormality of ALT/AST level) was not significantly associated with anti-HBs (Table 2).

The result of a suitable model for anti-HBs consisted of variables of HBsAg status and age group to see the relationship among those risk markers was shown on Table 3.

Table 1. Relationship of some characteristics to anti hepatitis B surface antigen (anti-HBs)

	Anti-HBs status				OR*	95% CI
	Positive (N=174)		Negative (N=821)			
	n	%	n	%		
Gender						
Male	80	46.0	381	46.4	1.00	(reference)
Female	84	54.0	440	53.6	1.02	0.72 - 1.43
Education						
High	41	23.6	171	20.8	1.00	(reference)
Middle	84	48.3	460	56.0	0.76	0.50 - 1.15
Low	48	27.6	186	23.8	1.07	0.67 - 1.71
Unknown	1	0.6	3	0.4	1.39	0.14 - 13.71
Socioeconomic status						
High	41	23.6	201	24.5	1.00	(reference)
Middle	31	17.8	174	21.2	0.87	0.53 - 1.45
Low	102	58.6	446	54.3	1.21	0.75 - 1.67
Ethnic group						
Malayan	161	92.5	744	90.6	1.00	(reference)
Chinese	13	7.5	77	9.4	0.78	0.40 - 1.49
Family size						
1-2 persons	53	30.5	225	27.4	1.00	(reference)
3-4 persons	67	38.5	325	39.6	0.88	0.59 - 1.30
5 persons and over	54	31.0	271	33.0	0.85	0.56 - 1.29
Alcohol use						
No	169	97.1	790	96.2	1.00	(reference)
Yes	5	2.9	31	3.8	0.75	0.29 - 1.97

* Univariate analysis

Table 2. Relationship of medical risk factors to anti hepatitis B surface antigen (anti-HBs) Anti-HBs status

	Anti-HBs status				OR*	95% CI
	Positive (N=174)		Negative (N=821)			
	n	%	n	%		
Ever had jaundice						
Never	166	95.4	776	94.5	1.00	(reference)
Ever	45	4.6	45	5.5	0.83	0.39 - 1.80
History of family jaundice						
None	151	86.8	703	85.6	1.00	(reference)
Yes	15	8.6	80	9.7	0.87	0.47 - 1.60
Unknown	8	4.6	38	4.6	0.98	0.41 - 2.24
Transfusion history						
Never	160	92.0	779	94.9	1.00	(reference)
Ever	14	8.0	42	5.1	1.62	0.87 - 3.04
History of operation						
Never	147	84.5	705	85.9	1.00	(reference)
Ever	27	15.5	116	14.1	1.12	0.70 - 1.76
Hepatitis B vaccination						
Never	116	85.3	627	95.6	1.00	(reference)
Ever	20	14.7	29	4.5		
AST †						
Normal	130	74.7	640	78.0	1.00	(reference)
Abnormal	44	25.3	181	22.0	0.82	0.45 - 1.49
ALT ‡						
Normal	160	92.0	742	90.4	1.00	(reference)
Abnormal	14	8.0	79	9.6	1.20	0.82 - 1.75
Hepatitis B surface antigen						
Negative	172	98.9	782	95.2	1.00	(reference)
Positive	2	1.1	39	4.8	0.23	0.06 - 0.98

* Univariate analysis

† AST, aspartate aminotransferase

‡ ALT, alanine aminotransferase

Compared to HBsAg negative subgroup, the positive HBsAg subgroup had lower risk of having a positive anti-HBs, adjusted odds ratio for age group was 0.24 (95% CI: 0.06-1.00; $p=0.051$).

Compared to subgroup 15-19 years and adjusted for HBsAg status, there was a positive overall trend of the relationship between age groups and anti HBsAg status (test for trend $p=0.004$). The risk was significantly increased beginning the age group of 30-39 years (adjusted OR=1.86; 95% CI: 1.01-3.42). The 40-49 years subgroup had 2.2 fold risk (adjusted OR=2.19; 95% CI: 1.21-3.69). And also the subgroup of 50-59 had risk of almost two times (adjusted OR=1.78; 95% CI: 0.96-3.32; $p=0.070$).

DISCUSSION

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 urban areas of Indonesia. Thus, our results may underestimate the prevalence of anti-HBs in urban populations. In addition, our population was limited to subjects age 15 and over and the results for younger children are not known. We do not have data on tattooing as well as intravenous drug abuse and sexual transmission.

Our study had a number of methodological strengths, including large size and a community-based design. However, our participation rate was quite high (89%), making it unlikely that selection bias has played any substantial role in our findings.

Table 3. Relationship of hepatitis B surface antigen and age groups to anti hepatitis B surface antigen (anti-HBs) Anti-HBs status

	Anti-HBs status				OR*†	95% CI
	Positive (N=174)		Negative (N=821)			
	n	%	n	%		
Hepatitis B surface antigen status						
Negative	172	98.9	782	95.2	1.00	(reference)
Positive	2	1.1	39	4.8	0.24	0.06 - 1.00 ‡
Age group						
15 - 19 years	19	10.9	133	16.2	1.00	(reference)
20 - 29 years	30	17.2	230	28.0	0.92	0.50 - 1.69
30 - 39 years	35	20.1	131	16.0	1.86	1.01 - 3.42
40 - 49 years	42	24.1	135	16.4	2.19	1.21 - 3.69
50 - 59 years	31	17.8	120	14.6	1.78	0.96 - 3.32
60 - 87 years	17	9.8	17	8.8	1.64	0.80 - 3.35

Test for trend: $p = 0.004$

* Odds ratio for hepatitis B surface antigen status adjusted for age group

† Odds ratio for age group adjusted for hepatitis B surface antigen status

‡ $p = 0.051$

The biggest number percentage of the sample were from the middle education level of 54.7%, followed by high education level of 21.3%. In general, only a small percentage of urban Indonesian people in 1994 who had middle education level was 13.6% and the high education level was 3.2%.⁷

The level of socioeconomic status of our subjects was higher than the average of general urban Indonesian people. Our data showed that the high socioeconomic level was 24.3%, and the middle class was 20.6%. Whereas in general, only a small number of urban Indonesian socioeconomic level with high socioeconomic status.⁷

Beside the risk marker of HBsAg, we studied other risk markers that have been reported to be associated with anti-HBs but none of these risk markers showed statistically significant associations. This non statistically difference was most likely due to a lower power. Anti-HBs in this study was not related to socioeconomic status. This situation might be due to almost half of the subjects come from middle and high classes and relatively bigger number of middle and higher educated people. In general, education related to health status, therefore most likely minimize the risk of developing hepatitis infection.

The seroprevalence of anti-HBs in this community-based study was 17.5% and HBsAg was 4.1%. It can be considered into consideration pattern of hepatitis B intermediate prevalence rate (where childhood infection frequent and neonatal infection infrequent).⁸

In this community-based study are different from blood donor surveys on the prevalence of viral hepatitis. The other study in 1990 which consisted of 243 voluntary blood donors was performed in Jakarta.³ They found the prevalence of HBsAg to be 5.8% and anti-HBs to be 32.9%. A large number of blood donor survey also found the prevalence of HBsAg among blood donors to be 5.5%.⁹ These differences illustrate the problems of comparing community-based studies with those derived from selected groups of blood donors.

Another community-based study consisted of 582 subjects in northern part of Jakarta (1995) where most of the subjects came from low socioeconomic status, low educated.¹⁰ They found the prevalence of anti-HBs and HBsAg were 25.0% and 2.7% respectively. The seroprevalence rates of anti-HBs was higher compared to our study. This may be due to different demographic characteristics (low socioeconomic class and lower

educated status), and different serologic methods. The northern part of Jakarta study was using Elisa serologic test, while our study, tests for anti-HBs was done using passive hemagglutination (PHA). Elisa serologic test is more sensitive test than PHA test.¹¹

Hepatitis B 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.^{8,9}

Our community-subjects with anti-HBs and HBsAg seroprevalence of 17.5% and 4.1% respectively can be considered into consideration pattern of hepatitis B intermediate prevalence rate, therefore active immunization remains as the most important method of achieving wide spread prevention and eventual elimination of hepatitis B.⁸ However, in order to maximize the benefit of immunization programs, it is necessary to be foci on the groups at high risk of hepatitis B virus (HBV) infection.

Our data revealed there is a significant positive trend (adjusted test for trend: $p = 0.004$) between age group and risk of anti-HBs positive. The test for trend was adjusted for HBsAg status. This finding was similar with the northern part of Jakarta study.

Among our subjects aged of 15-19 years, only 19 out of 152 (12.5%) persons positive for anti-HBs (Table 3). Since this small number of immune young ages toward HBV, and the seroprevalence of anti-HBs among and HBsAg among our subjects can be considered into intermediate, therefore HBV vaccination should be targeted to adolescents among our subjects. Selected vaccination of adolescents who had anti-HBs negative can be carried out by community health facilities and family physicians.¹²

Family physicians can have a mayor influence on the success of this immunization strategy, because family physicians provide comprehensive family health for their community, including obstetric, perinatal, adolescent and adults care, and most likely more familiar to the risk of hepatitis B infection among their clients.

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