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Increasing Susceptibility to HAV among Members of the Young Generation in Thailand

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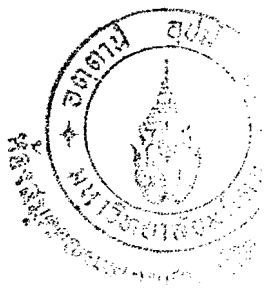

SUMMARY **The prevalence of antibodies to hepatitis A virus was studied in 961 children and adolescents, randomly selected from five different provinces in Thailand (Chonburi, Lopburi, Udonthani, Nakhon Si Thammarat and Lopburi). The highest prevalence was found in Nakhon Si Thammarat, with 32.1 percent of those aged 10-14 years and 57.1 percent of those aged 15-18 years showing evidence of protective immunity. However, this high rate could be explained by an outbreak of hepatitis A in 1992. In the remaining four provinces, the pattern was typically age-related in that all individuals showed between zero and 13 percent antibody prevalence until reaching the 15-to-18-year age group where it increased to between 5.6 and 22.7 percent. The overall sero-prevalence among all age groups was 7.9 percent. Thus, the majority of the younger generation is susceptible to hepatitis A virus infection thereby enhancing the impact, should an outbreak occur. Preventive measures that might be taken are education aimed at better hygiene and sanitation, as well as vaccination of susceptible individuals within high-risk populations.**

The hepatitis A virus is a single-stranded RNA molecule belonging to the family *Picornaviridae*. The virus is characterized by exceptional stability to physiological pH, temperature and environment. It has the ability to survive in fresh as well as sea water for several weeks.[1] Based on these characteristics, HAV ranks as one of the most stable viruses and is easily transmitted by contaminated water, food and fecal material, under both endemic and epidemic conditions. This situation is rendered even more severe by apparently increased resistance of HAV to chlorinating, a feature differentiating it from common picornaviruses.[2]

Although numerous strains of human hepatitis A virus have been described, they appear immunologically indistinguishable and hence, have been grouped into one serotype. So far, all epitopes identified on the surface of HAV seem to be closely spaced and part of a single immunodominant neutralization site, which is highly conserved among all wild-type isolates of HAV described to date.[3]

HAV infection in infants and young children is usually asymptomatic, leaving them with life-long immunity. However, with advancing age it is characterized by clinical symptoms of increasing severity. Except for those cases where hepatitis A appears as a super-infection of pre-existing chronic hepatitis B and/or C disease,[4] the mortality rate as a consequence of hepatitis A infection is low.

The prevalence of hepatitis A is closely related to the respective socio-economic development in any given area so that the frequency of anti-HAV is inversely related to

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the socio-economic status of the populations investigated.[5] Even so, in countries with the lowest living standards, the highest population densities along with the poorest hygiene and sanitation, vaccination against HAV is not yet indicated. Among these populations, infection is usually acquired during infancy or early childhood and follows an asymptomatic course without leaving any long-term sequelae.[6] In developed countries, the disease is not evenly distributed within the population and the primary targets for vaccination comprise members of high risk groups, such as individuals frequently travelling overseas or those with compromised immune response.

Due to recent improvements in living conditions leading to a shift from childhood infections to adult infections, hepatitis A has recently become a major problem in many developing countries. In Thailand, where the socio-economic situation has experienced a continuous progression towards that of a newly industrialized country, the frequency of hepatitis A infection among children has been decreasing within recent years. Accordingly, there has been an increasing number of symptomatic HAV infections among the adult populations.[7]

HAV infections affect population groups depending on their respective lifestyle and geographical location. Hence, epidemiological studies ought to be performed on various populations, selected on the basis of their socio-economic background and area of residence, in order to define the extent of the threat to public health and to devise the necessary preventive measures accordingly. Therefore, the main purpose of the present study is to establish the prevalence of anti-HAV among children and adolescents in different parts of Thailand.

MATERIALS AND METHODS

Population Study

The populations studied were part of a separate research project regarding the impact of the universal mass vaccination program against hepatitis B virus (HBV) infection. Samples were collected in 5 representative provinces in Thailand: Chonburi (81 km to the east of Bangkok), Lopburi (153 km to the north, in the central region), Udonthani (564 km to the northeast), Nakhon Si Thammarat (780 km to the south) and Lampang (599 km to the north). The majority of the population in these provinces live in rural agricultural areas. From approximately 400-488 specimens per area, which were collected for determination of hepatitis B virus markers, we randomly selected 191-195 samples per province for detection of anti-HAV antibodies. The samples were stratified by age, i.e., between 1-4, 5-9, 10-14 and 15-18 years. Further details, as well as the male/female distribution of the subjects examined are depicted in Table 1. In order to be included in the study, the subjects had to be of general good health; they had to be free from any chronic illness; they were not supposed to be receiving immunosuppressive therapy; they also had to be free from clinical signs or symptoms associated with either HIV infection or any immunodeficiency of different etiology. Before taking blood samples, all participants were informed as to the purpose of the study and their written informed consent was subsequently obtained.

Laboratory methods

Sera were separated by centrifugation and kept at -20°C until tested. A total of 961 specimens were tested by enzyme-linked immunosorbent assay for anti-HAV antibodies using a commercially available ELISA kit (HAVAB, Abbott Laboratories, North Chicago, Ill.). The cut-off level for immunity to HAV was calculated as specified by the manufacturer.

Data analysis

Data were analyzed by determining the percentages of anti-HAV antibodies obtained for each age group in each area.

RESULTS

In all individuals of provinces examined, except for Nakhon Si Thammarat, anti-HAV antibody levels detected among all age groups ranged between zero and 8.2 percent. In general, the prevalence of anti-HAV antibodies showed an age dependent increase typical for areas in transition from underdeveloped to newly industrialized status. There was a rise in levels from 5.6 percent in the 10-14-year age group to 13.5 percent in the 15-18-year age group in Lopburi, from 1.8 to 22.7 percent in Udonthani and from zero to 11.4 percent in Lampang. However, in Chonburi, the highest percentage (13.0) was observed within the 1-4-year age group, which declined to between 3.7 and 7.0 percent in the older age groups. In Nakhon Si Thammarat, the anti-HAV prevalence rose from 4.1 in the 1-4-year age group to 32.1 percent in the 10-14-year age group, and further increased to 57.1 percent within the 15-18-year age group. The overall sero-prevalence rate among children and adolescents was determined to be 7.9 percent. The details are shown in Fig. 1 and Table 2.

Table 1 Population examined for anti-HAV per province

Location	Population studied for impact of HBV vaccination	Population randomly chosen for anti-HAV test	Male	Female
Chonburi	457	193	118	75
Lopburi	488	191	82	109
Udon Thani	400	195	87	108
Nakhon Si Thammarat	472	191	82	109
Lampang	413	191	90	101
Total	2,230	961	459	502

Table 2 Details of anti-HAV prevalence as to age group and province

Age group (Years)	Chonburi		Lopburi		Udon Thaini		Nakhorn Si Thammarat		Lampang		Total	
	No.	Anti-HAV No. (%)	No.	Anti-HAV No. (%)	No.	Anti-HAV No. (%)	No.	Anti-HAV No. (%)	No.	Anti-HAV No. (%)	No.	Anti-HAV No (%)
1-4	46	6 (13.0)	45	2 (4.4)	39	0 (0)	49	2 (4.1)	41	0(0)	220	10 (4.5)
5-9	54	2 (3.7)	55	2 (3.6)	57	5 (8.8)	68	3 (4.4)	53	0(0)	287	12 (4.2)
10-14	57	4 (7.0)	54	3 (5.6)	55	1 (1.8)	53	17 (32.1)	53	0(0)	272	25 (9.2)
15-18	36	2 (5.6)	37	5 (13.5)	44	10 (22.7)	21	12 (57.1)	44	5(11.4)	182	29 (15.9)
Total	193	14 (7.3)	191	12 (6.3)	195	16 (8.2)	191	34 (17.8)	191	5 (2.6)	961	76 (7 9)

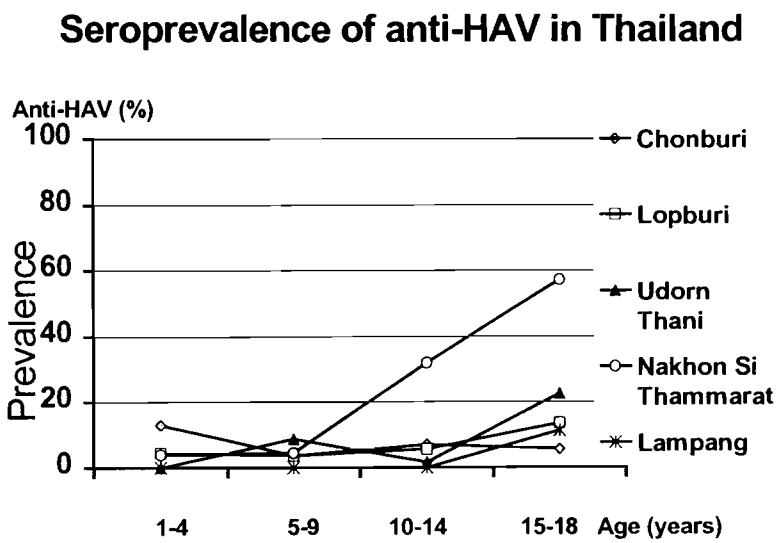

Fig. 1 Sero-prevalence of anti-HAV in relation to age groups and individual provinces in Thailand.[1]

DISCUSSION

Until the early 1980s, Thailand has been a country hyperendemic for hepatitis A. In the course of the past two decades, profound changes from a developing to a new industrialized country have increasingly taken place, affecting the socio-economic conditions of the population, mainly in urban and suburban areas. The subsequent improvement in living standards has been paralleled by better education leading to improved hygiene and sanitary conditions. Consequently, fecal-orally transmitted infections such as typhoid, cholera and hepatitis A, have acquired an intermediate endemic pattern. Hence, infections that used to affect infants

and young children and to follow, with few exceptions, an entirely asymptomatic course have shifted towards the adolescent or adult populations, where due to a total lack of immunity on the patients' part clinical symptoms tend to become more severe with increasing age.[8] Comparable developments have been observed in other newly industrialized countries such as Taiwan and Singapore, where the prevalence of HAV infection has also undergone a shift from hyperendemic to intermediate endemic.[9,10] Generally, in any country where a major part of the population is susceptible to the hepatitis A virus, the risk of an endemic occurring is heightened, as exemplified by the 1988 outbreak in Shanghai.[11,12] Several years ago, an outbreak of infection transmitted by one index case was detected among radio-technology students at Chulalongkorn Hospital in Bangkok. The outbreak, fortunately, could be contained.[13]

The present study has been conducted in order to establish the prevalence and age-related pattern of anti-HAV antibodies among young children and adolescents in five regions of Thailand: Chonburi, Lopburi, Udonthani, Lampang and Nakhon Si Thammarat. Most of these provinces are rural agricultural areas. Except for Nakhon Si Thammarat, all areas displayed a prevalence of anti-HAV antibodies, which is characteristic for regions in transition from developing to newly industrialized countries, in that prevalence was clearly age-dependent. There was a very low frequency among the younger age groups of 1-4, 5-9 and 10-14 years, with a gradual increase in the 15-18-year age groups. However, the data for Chonburi showed that the prevalence also remained low in this age group (Table 2).

Similar trends have been reported from Hong Kong[14] and among the Chinese people living in urbanized areas with improved sanitation and living standards,[10,15] as well as in several developed countries in other parts of the world.[16,17] In Thailand, in the course of previous studies, our group has repeatedly been confronted with identical patterns, regardless of whether they were among children or adolescents, in urban or in rural communities.[18-20] One consequence of this development was manifested in 1992 by a massive outbreak of hepatitis A in Nakhon Si Thammarat. The prevalence rate was 5 times the average and caused a profound public health burden.[21] The anti-HAV prevalence established for Nakhon Si Thammarat in the present study bears witness to this epidemic, in that measurable immunity shows a sharp increase in the 10-14-year age group, with a further sharp increase to almost double that percentage among the 15-18-year age group (Table 2).

Based on these observations, we conclude that in areas with populations susceptible to HAV infection, vaccination against hepatitis A is recommended in addition to the appropriate health education aimed at improving hygiene and sanitation, especially as the entire range of currently available vaccines has been proven highly immunogenic and devoid of any serious adverse effects. Based on the presently high cost of the vaccine in developing countries, it ought to be administered to certain high risk groups, such as children and staff in day-care facilities, travelers, military personnel and health care personnel in infectious wards. Before expanding vaccination to the population at large, its cost-effectiveness certainly needs to be evaluated.

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