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Seroepidemiological study of HBV infections in Athens, Greece

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SUMMARY

A seroepidemiological survey of a sample – roughly representative by age and sex – of 2744 persons of the Greater Athens area revealed that hepatitis B virus (HBV) infections are highly endemic in Greece. Hepatitis B surface antigen (HBsAg) was detected in 72 (2·6 %) of them. The subtype was identified in 70 of the 72 carriers, and 69 were ay; the other was ad. Determinant w was present in all 61 that were capable of being typed further, and $a_2$3y(w) was twice as common as $a_1$1y(w). Antibody to HBsAg (anti-HBs) was found in 514 (18·7 %) persons. The prevalence of the HBsAg rose rapidly with age, reaching peak values (5·3 %) at 20–29 years, while anti-HBs reached its highest value (42·1 %) in older age groups (50–59 years). The frequency of HBsAg was significantly higher in males (3·4 %) than in females (1·5 %). The percentage of infected persons who become chronic HBsAg carriers (12·3 %) was found higher than in other developed populations. It was also found higher in children (25 %) than in adults (5·5 %) and in males (14·6 %) than in females (8·1 %). These data indicate that HBV infection in early life is a major risk factor in the development of HBsAg carriers and support the hypothesis that males are more likely to become HBsAg carriers than females.

INTRODUCTION

Viral hepatitis has been considered as a major public health problem in Greece. The application of serological techniques for the detection of HBV infections provided further evidence for the high endemicity as well as for some epidemiological characteristics of the disease. However, the majority of investigations concerned self-selected samples of people which were incomplete as regards age and sex (Papaevangelou, Vissoulis, Kremastinou & Trichopoulos, 1974). To provide further information on the prevalence as well as certain other epidemiological features of HBV infections we studied by sensitive serological techniques a sample of 2744 persons, roughly representative of the population of the Greater Athens area. The results of this study are reported in the present paper.

MATERIALS AND METHODS

The age-stratified sample studied consisted of 2744 lifetime residents of the Greater Athens area. Sixteen hundred and nine of them were males and 1135 females. Their distribution by sex and age is shown in Tables 1, 2 and 3. The

Table 1. *Hepatitis B surface antigen (HBsAg) and antibody (anti-HBs) prevalence rate by age in the Athens area*

Age (years)	Total number	HBsAg		Anti-HBs		HBsAg + anti-HBs		Percentage carriers*
		Positive	%	Positive	%	Positive	%	
0–4	37	1	2·7	3	8·1	4	10·8	25·0
5–9	408	3	0·7	14	3·4	17	4·2	17·5
10–14	643	10	1·6	71	11·0	81	12·6	12·3
15–19	421	14	3·3	84	19·9	98	23·3	14·3
20–29	531	28	5·3	125	23·5	153	28·8	18·3
30–39	162	8	4·9	42	26·0	50	30·9	16·0
40–49	208	4	1·9	59	28·4	63	30·3	6·4
50–59	152	1	0·7	64	42·1	65	42·8	1·5
60+	182	3	1·6	52	28·6	55	30·2	5·5
Total	2744	72	2·6	514	18·7	586	21·3	12·3

* Percentage carriers: HBsAg carriers/Anti-HBs + HBsAg carriers.

sample was collected from November 1973 to March 1975 as follows. Children 0–4 years old were selected from Child Welfare Centres. Elementary and high schools of various districts of Athens were used for the collection of sera from persons 5–19 years old. The sample for persons older than 20 years was completed from Air Force recruits, volunteer blood donors as well as outpatients and patients entering the Red Cross Hospital for reasons other than chronic or liver diseases. Thus the sample should be considered as roughly representative of the population of the Greater Athens area as regards age, sex, social class and geographical location. Environmental and medical history data were collected and a venous blood specimen was drawn under aseptic conditions. Sera were frozen until tested.

HBsAg was detected by counterimmunoelectrophoresis by the method of Pesendorfer, Krassnitzky & Wewalka (1970). The WHO reference antiserum (caprine) to HBsAg was used. Antigenic subspecificities ad and ay were determined by immunodiffusion (Le Bouvier & McCollum, 1970) using monospecific antisera, kindly provided by Dr Overby. Further subspecificities were kindly determined by Dr A. M. Couroucé.

Screening for anti-HBs was done by passive haemagglutination assay (PHA). HBsAg coated red blood cells were provided by Virgo Reagents, Electronucleonics Laboratories, Inc., U.S.A. PHA titres of 1/8 or greater were considered positive. Differences between frequency rates were tested by χ^2 test with Yates's correction for small numbers.

RESULTS

HBsAg was detected in 72 (2·6 %) and anti-HBs in 514 (18·7 %) out of 2744 persons studied. Anti-HBs was not detected in any of the HBsAg positive sera. Thus, the serological evidence of HBV infection (combined HBsAg and anti-HBs prevalence) was found in 21·3 %. The prevalence of HBsAg, anti-HBs and sero-

Table 2. *Hepatitis B surface antigen (HBsAg) and antibody (anti-HBs) prevalence rate mong males by age in the Athens area*

Age (years)	Total examined	HBsAg		Anti-HBs		HBsAg + anti-HBs	
		Positive	%	Positive	%	Positive	%
0–4	21	1	4·8	2	9·5	3	14·3
5–9	205	2	1·0	4	1·9	6	2·9
10–14	373	6	1·6	51	13·7	57	15·3
15–19	234	10	4·3	46	19·6	56	23·9
20–29	378	22	5·8	96	25·4	118	31·2
30–39	106	7	6·6	29	27·4	36	34·0
40–49	113	3	2·6	31	27·4	34	30·0
50–59	97	1	1·0	36	37·1	37	38·1
60+	82	3	3·6	26	31·7	29	35·4
Total	1609	55	3·4*	321	19·9†	376	23·4

* HBsAg age-adjusted prevalence rate: 3·3 %.
† Anti-HBs age-adjusted prevalence rate: 19·0 %.

Table 3. *Hepatitis B surface antigen (HBsAg) and antibody (anti-HBs) prevalence rate among females by age in the Athens area*

Age (years)	Total examined	HBsAg		Anti-HBs		HBsAg + anti-HBs	
		Positive	%	Positive	%	Positive	%
0–4	16	—	—	1	6·2	1	6·2
5–9	203	1	0·5	10	4·9	11	5·4
10–14	270	4	1·5	20	7·4	24	8·9
15–19	187	4	2·1	38	20·3	42	22·4
20–29	153	6	3·9	29	18·9	35	22·9
30–39	56	1	1·8	13	23·2	14	25·0
40–49	95	1	1·0	28	29·5	29	30·5
50–59	55	—	—	28	50·9	28	50·9
60+	100	—	—	26	26·0	26	26·0
Total	1135	17	1·5*	193	17·0†	210	18·5

* HBsAg age-adjusted prevalence rate: 1·7 %.
† Anti-HBs age-adjusted prevalence rate: 19·2 %.

logical evidence of HBV infection by age is shown in Table 1. The frequency of both HBsAg and anti-HBs increased with increasing age except for a relatively high prevalence in the age group 0–4 years old. HBsAg prevalence reached its highest level at the age group 20–29 years (5·3 % positive) and then it declined in the older age groups. In contrast, anti-HBs continued to increase up to the 50–59 age group (42·1 %) and slightly declined in older persons (28·6 %).

The age- and sex-specific prevalence rates of HBsAg and anti-HBs are shown in Tables 2 and 3. There was a significantly higher HBsAg prevalence in males (3·4 %) than in fem ales (1·5 %); ($\chi^2 = 8{\cdot}9, P < 0{\cdot}01$). Fig. 1 shows that the frequency of HBsAg was higher in males than in females in every age group. There was no significant difference between the total anti-HBs prevalence in males (19·9 %) and

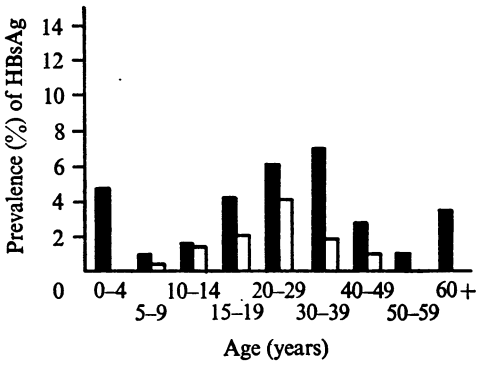

Fig. 1

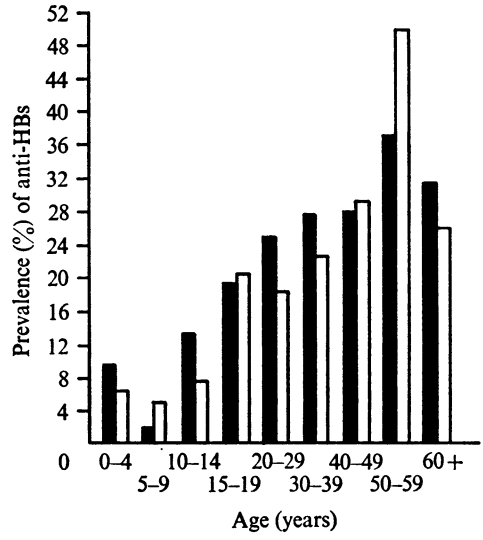

Fig. 2

Fig. 1. Age- and sex-specific prevalence rate of Hepatitis B surface Antigen (HBsAg). ■, Males; □, females.

Fig. 2. Age- and sex-specific prevalence rate of antibody to Hepatitis B surface Antigen (anti-HBs). ■, Males; □, females.

females (17 %), and the prevalence was similar or slightly higher in males or females in the various age groups (Fig. 2).

Age adjustment did not substantially change the male or female HBsAg and anti-HBs prevalence rate (Tables 2, 3). The percentage of persons actually infected with HBV who became HBsAg carriers (percentage of carriers = HBsAg carriers/anti-HBs + HBsAg carriers) was found to be 12·3 %. This was highest in children 0–4 years old (25 %) and declined substantially in older persons (1·5–5·5 %; Table 1). It was also significantly ($\chi^2 = 4{\cdot}74$, $P < 0{\cdot}05$) higher in males (55/376 or 14·6 %) than in females (17/210 or 8·1 %).

Subspecificities

HBsAg subtypes could be determined in 70 (97·2 %) of the 72 carriers. All except one were subtype ay. Eight ay subtypes were antigenically very weak for further subspecification. In the remaining 61, the third determinant w could be defined and $a_2$3y(w) was twice as common as $a_1$1y(w) (41:20).

DISCUSSION

The pattern distribution of HBV infections in the population studied indicates that viral hepatitis B is highly endemic in Greece. Almost 50 % of persons 50–59 years old showed serological evidence of HBV infection. However this should be considered as an underestimate of the HBV infection rate, since the methods used are not the most sensitive for the detection of HBsAg and anti-HBs. Moreover evidence has been provided that loss of serological evidence of HBV infections as

well as reinfections are common events, so that HBV infection prevalence by age cannot ever reach 100 % (Grossman *et al.* 1975). Similar high rates have been reported only for institutionalized populations as well as for populations of Africa and the Far East (Szmuness *et al.* 1973), but the reported rates for U.S.A. and Western European populations were substantially lower (Cherubin *et al.* 1972; World Health Organization, 1973).

Only a very small proportion of persons with serological evidence of past HBV infection had a history of jaundice. The results of this study in accordance with previous reports (Papaevangelou *et al.* 1974) suggest that clinically inapparent infections by HBV are very common in this population.

The age curve of HBsAg prevalence has a pattern similar to that of other populations (Vissoulis & Papaevangelou, 1973). However, peak values happen in Greece at an earlier age (20–29 years) than in other developed countries, probably because of the higher transmission rates in Greece (Szmuness *et al.* 1975). The high HBsAg prevalence rate in the few children under four years old may be attributed to the early intimate contact with HBsAg carrier mothers or other family members. It may also probably represent a fortuitous occurrence within the realm of sampling effect because of the small numbers at that age group.

A substantial proportion (12·3 %) of those infected with HBV became chronic HBsAg carriers. This should be considered as an overestimate, because of the loss of anti-HBs in a considerable proportion of the infected persons. However, the 12·3 % of carriers found is substantially higher than the 1·8–3·5 % calculated for the U.S.A. adults and lower than that for populations of tropical and underdeveloped countries (28–40 %), as well as for institutionalized children (35·7 %) (Gerety, Hoofnagle, Markenson & Barker, 1974).

In accordance with other reports the percentage of carriers in children was found higher than in adults (Table 1). These data support the hypothesis that HBV infection in early life is a major risk factor in the development of chronic HBsAg carriers (Krugman & Giles, 1973). They indicate also that the age at which transmission occurs determines not only the total HBsAg prevalence rate, but also the shape of its age curve.

The higher prevalence of HBsAg found in males than females should not be attributed to a greater risk of exposure, since the percentage of carriers was higher in males (14·6 %) than in females (8·1 %). These data support the hypothesis that males are more likely to become HBsAg carriers than females (Blumberg, Sutnick, London & Melartin, 1972). Males may be also less capable of eliminating the HBsAg. This may lead to chronic aggressive viral hepatitis and sometimes terminate in liver-cell carcinoma, both of which are indeed more prominent in males than females (Sherlock, Fox, Niazi & Scheuer, 1970; Hadziyannis, 1974).

The subtypes of HBsAg seem to be of great epidemiological relevance and importance. Major geographical differences in the distribution of the y, d and w,r antigenic determinants have been reported (Le Bouvier, 1971; Bancroft, Mundon & Russel, 1972; Mazzur, Burgert & Blumberg, 1974; Mosley, Edwards, Meilhaus & Redecker, 1972). As previously reported the great majority of HBsAg in Greece are ay (Hadziyannis & Le Bouvier, 1972). Furthermore, as expected, only the w

determinant was found in the present study. Thus, determination of these subtypes cannot serve in Greece as epidemiological markers for investigating the routes of transmission and other epidemiological characteristics of the disease. According to the results of this study heterogeneity exists in the subdeterminants of the common a determinant, which may serve as markers for certain definitive epidemiological studies of HBV transmission, expression of infection and chronic carrier state in Greece.

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