ORIGINAL CONTRIBUTION

Prevalence of Hepatitis B Virus Infection Markers Among a Working Population in a Coastal City of Yantai, China

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Three markers of hepatitis B virus (HBV) infection, HBsAg, anti-HBs and anti-HBc, were investigated in the sera from 426 factory workers of both sexes in a coastal city of Yantai in China. The investigation showed that the rate of those positive to HBsAg was 25.4% (25.9% in men and 24.6% in women), and that the rate when two sexes were combined was highest (i.e., 29.5%) at the ages of 20s followed by gradual decrease at higher ages (below 20%). The overall HBV infection rate as calculated by those positive to any of the three markers studied was 70.4%. Comparison with rates reported in literature indicated that the rate of HBsAg-positive cases in the present study are probably among the highest values in China, whereas overall rate of HBV infection was almost comparable to the values for other provinces. It should be added that other reports on other parts of Shandong Province describe HBsAg prevalence of about 6%. No explanation is currently available for the high HBsAg prevalence among the study population. J Epidemiol, 1991; 1: 11-17.

anti-HBc, anti-HBs, China, HBsAg, HBV

Persistent infection of hepatitis B virus (HBV) is among the known risk factors of primary hepatocellular carcinoma (PHC). Accordingly, increasing attention has been given in public health to the prevalence of the HBV infection with intention for the prevention of this insidious disease1-7). It is generally understood that the prevalence is higher in many parts of the Asian and Pacific regions than in northern Europe and North America8-10). Reports on HBV prevalence in China are also growing in numbers reflecting the large population, with focus to the areas of high PHC incidence such as Guangxi Province6,11-15).

In continuation of seroepidemiological surveys by this study group on HBV infection in East Asia16-19), a study was conducted in a coastal city of Yantai in Shandong Province, China, the area where there still exists a paucity of data on HBV infection.

MATERIALS AND METHODS

Sera. In 1991, the survey was conducted in a port city of Yantai in Shandong Province, on the north coast of the Shandong Peninsula, as a part of an occupational health survey of factory workers. The workers both in production sections and in clerical sections were invited to participate in the study, and sera obtained from 426 workers (243 men and 183 women at the ages of 17 to over 50 years) were subjected to the seroepidemiological study.

HBV marker assays. The radioimmunoassay kits for 3 markers, i.e., AUSTRIA® 11-125 for HBsAg, AUSAB™ for Anti-HBs, and ANTI HBc RIAKIT™ for Anti-
HBc, were supplied by Abbott Laboratories (North Chicago, IL, USA). The cutoff indices for the identification of positive cases (to be abbreviated as HBsAg+, Anti-HBs+, and anti-HBc+) were set at >5, >2, and >70%, respectively.

Statistical evaluation. Statistical significance of difference in prevalence was evaluated by means of chi-square test.

RESULTS

Prevalence of the 3 HBV infection markers among the study population

The prevalence of cases positive to the three markers are summarized in Tables 1 and 2. Those positive to

Table 1. Prevalence of hepatitis B virus (HBV) infection markers among factory workers in Yantai.

| HBV infection marker | Number of cases | |
|----------------------|-----------------|---|
| HBsAg               | Men             | Women |
|                     | 64 (29.6)       | 62 (33.9) |
| Anti-HBs            | 12 (4.9)        | 4 (2.2)  |
| Anti-HBc            | 25 (10.3)       | 14 (7.2) |
|                     | 79 (32.5)       | 58 (31.7) |
|                     | 37 (11.1)       | 24 (13.1) |
|                     | 3 (1.2)         | 2 (1.1)  |

In total, 426 adults (243 men and 183 women) were studied. The numbers in the table are the numbers of cases and the percentages in parentheses. + : Positive. – : Negative.

Table 2. Prevalence of HBsAg+, anti-HBs+ and anti-HBc+ cases by age and by sex.

| Sex range (years) | No. of sera tested | HBsAg+ | Anti-HBs+ | Anti-HBc+ | Anti-HBs+ or Anti-HBc+ | Over-all+ | HBV marker negativea |
|-------------------|--------------------|--------|-----------|-----------|------------------------|-----------|----------------------|
| Men               |                    |        |           |           |                        |           |                      |
| 15-19             | 16                 | 3 (18.8)| 6 (37.5)  | 9 (56.3)  | 10 (62.5)              | 6 (37.3)  |                      |
| 20-29             | 168                | 51 (30.4)| 50 (29.8)| 92 (54.8)| 96 (57.1)              | 117 (69.6)| 31 (30.4)            |
| 30-39             | 34                 | 5 (14.7)| 21 (59.2)| 18 (52.9)| 24 (70.6)              | 28 (82.4)| 6 (17.6)             |
| 40-49             | 18                 | 2 (11.1)| 14 (77.8)| 16 (88.9)| 18 (100.0)             | 18 (100.0)| 0 (0.0)              |
| ≥50               | 7                  | 2 (28.6)| 3 (42.9)  | 5 (71.4)  | 5 (71.4)               | 6 (85.7)  | 1 (14.3)             |
| Total             | 243                | 93 (38.7)| 140 (57.6)| 152 (62.6)| 179 (72.7)             | 64 (26.3) |                      |
| Women             |                    |        |           |           |                        |           |                      |
| 15-19             | 22                 | 7 (31.8)| 6 (27.3)  | 7 (31.8)  | 8 (36.4)               | 13 (59.1) | 9 (40.9)             |
| 20-29             | 86                 | 24 (27.9)| 27 (31.4)| 38 (44.2)| 40 (46.5)              | 34 (40.4) | 32 (37.2)            |
| 30-39             | 37                 | 8 (21.6)| 15 (40.5)| 21 (56.8)| 21 (56.8)              | 25 (67.6)| 12 (32.4)            |
| 40-49             | 24                 | 4 (16.7)| 9 (37.5)  | 16 (66.7)| 17 (70.8)              | 18 (75.0)| 6 (25.0)             |
| ≥50               | 14                 | 2 (14.3)| 7 (50.0)  | 11 (78.6)| 11 (78.6)              | 3 (21.4)  |                      |
| Total             | 183                | 45 (24.6)| 64 (35.0)| 93 (50.8)| 97 (53.0)              | 121 (66.1)| 62 (33.9)            |
| Men and women combined |           |        |           |           |                        |           |                      |
| 15-19             | 38                 | 10 (26.3)| 12 (31.6)| 16 (42.1)| 17 (44.7)              | 23 (60.5) | 15 (39.5)            |
| 20-29             | 254                | 75 (29.5)| 77 (27.6)| 130 (51.2)| 136 (53.5)             | 171 (67.3)| 83 (32.7)            |
| 30-39             | 71                 | 13 (18.3)| 36 (50.7)| 39 (54.9)| 45 (63.9)              | 53 (74.6)| 18 (25.4)            |
| 40-49             | 42                 | 6 (14.3)| 23 (54.8)| 32 (76.2)| 32 (83.3)              | 36 (85.7)| 6 (14.3)             |
| ≥50               | 21                 | 4 (19.0)| 10 (47.6)| 16 (76.2)| 16 (76.2)              | 17 (80.9)| 4 (19.0)             |
| Total             | 426                | 108 (25.4)| 158 (37.1)| 233 (54.7)| 249 (58.5)             | 300 (70.4)| 126 (29.6)|

The values in the table are the number of cases and the percentages in parentheses. + : Positive. * Positive to either anti-HBs or anti-HBc. * Over-all rate of infection as defined by the rate of these positive to any of the 3 markers. a Negative to all of the 3 markers tested.
HBsAg accounted for one fourth of the population studied with no significant difference in the prevalence between the two sexes (p > 0.10), and about a half of the HBsAg+ people were negative to the 2 antibody items. In contrast, about one third of the people studied were anti-HBs+ and anti-HBc+ in both sexes, and somewhat less than one third was negative to all of the 3 infection markers (Table 1). Thus, well over two thirds of the study population were either currently or previously infected with HBV.

Very few (1%) were positive to all the three markers, as theoretically expected. In such cases, they were very weakly anti-HBs+ with titers just above the cut-off point, whereas anti-HBc titers were high and HBsAg titers were various depending on the cases.

Age-dependent changes in HBV infection rates

The observed cases were further classified by sex and by decade of years of ages of the subjects (Table 2). There is a gradual age-dependent decrease in HBsAg+ prevalence both in men and women, albeit the rate for those at the ages of 19 years or less (18.8% for men and 31.8% for women) may be comparable to that for 20s; no significant difference in the prevalence was detected between those at less than 20 years of age and those at 20-29 years, when the two sexes were combined (p > 0.10). A high rate of 28.6% for > 50 year-old men should be considered not reliable because only 7 subjects were examined.

Both anti-HBs+ and anti-HBc+ rates gradually increased in parallel in both sexes as ages advanced, so that about 80% or more of the population acquired immunity to HBV infection at the age of 40 years (i.e., either anti-HBs+ or anti-HBc+, or anti-HBs+ and anti-HBc+). When positive reaction in any of the three infection markers (i.e., HBsAg+, anti-HBs+ or anti-HBc+) was considered to be indicative of past or current HBV infection, almost all subjects (more than 85%) had experienced HBV infection before the age of 50, whereas less than 15% of the people remained negative to any of the three HBV infection markers at this stage of life.

DISCUSSION

The present study of a Yantai population has shown that the rate of those positive to HBsAg was as high as 25.4% (25.9% in men and 24.6% in women), and that the rate when two sexes were combined was highest (i.e., 29.5%) at the ages of 20s followed by gradual decrease at higher ages (about 20% or less). The overall HBV infection rate as calculated by those positive to any of the three markers studied was 70.4%.

A growing number of papers have been published in recent years to report the prevalence of HBV infection especially in terms of HBsAg+, and in some cases as the positivities to the three infection markers, in various cities and provinces in China, Taiwan, Guangxi Province where PHC mortality is known to be very high especially in men; the values higher than the present observation are usually associated with known HBV infection or inclusion of hepatitis cases.

The anti-HBs+ and anti-HBc+ rates were not remarkably high so that the overall rate of HBV infection of the present study population is only comparable to the values for other provinces. It was previously pointed out that the prevalence of HBV infection is lower in a large city like Beijing (although not in Shanghai where PHC mortality is reported to be high) than in rural provinces. Simple urban-rural difference, however, will not be sufficient to explain rather unusually high HBsAg rate among the working population in the present study (Tables 1 and 3).

For comparison with the present observation, 6 reports are available in addition to an early report of Beasley and his co-workers on HBV infection in Shandong Province in particular. The reported HBV infection prevalence as defined by positive to any of the 3 markers reported in recent studies are in a wide range of 27.4% to 78.3%. Nevertheless, the prevalence of HBsAg+ cases are all well below 10%.

Beasley et al. found that the HBsAg+ prevalence among former Shandong Province residents currently in Taiwan were 9.3%, the value being not higher as compared with the values for those from northern China (11.2% on an average) and probably lower than the values for those from southern China (17.5%). In agreement with rather low HBsAg+ prevalence, the rates of mortality from liver cancer (per 10^5 population, based on deaths in 1973 to 1975, and age-adjusted to 1964 census population of China) was 11.57 for men (4.24 for women) in Shandong Province; the values are not higher than the values for the whole country (14.52 for men and 5.61 for women), and quite lower than those for Guangxi Province (26.55 for men and 6.63 for women) where HBV infection prevalence...
is also high (Table 3). Thus, it could be the case that the HBV infection prevalence is specifically high in the present study population, even though the prevalence may be generally low in Shandong Province; such may be quite probable bearing in mind that Shandong Province has a large population of 80 millions in a large area of 150,000 km².

The age-dependent changes in HBsAg prevalence of the present study population in Yantai is depicted in comparison with the counterpart observation in Beijing, Shanghai, Wuxi, Xian and Hefei made by the present study group in Figure 1; a high prevalence (33%) observed in less than 20 year-old subjects in Wuxi may be due to the fact that only a small number of people (15 subjects) were examined in this age group, and therefore not depicted in the figure. It is apparent from Figure 1 that the prevalence in Yantai subjects up to 49 years of age is much higher than their

| Study area | Population | Assay by R or H | HBV infection marker positive (%) | Reference |
|------------|------------|----------------|-----------------------------------|-----------|
| Anhui      | 503 Factory workers | R          | HBsAg 8, Anti-HBs 46, Anti-HBe 53, Over-all 53 | 16        |
| Beijing    | 398 All ages | R          | HBsAg 7, Anti-HBs 20, Anti-HBe 26 | 20        |
| Ibid.      | 600 Dental workers | H          | HBsAg 6, Anti-HBs 37, Anti-HBe 46 | 22        |
| Ibid.      | 491 All ages | R          | HBsAg 7, Anti-HBs 37, Anti-HBe 44 | 17        |
| Fujian     | 407 Children (1979) | H          | HBsAg 17, Anti-HBs, Anti-HBe | 23        |
| Ibid.      | 6558 Children (1987) | H          | HBsAg 7, Anti-HBs, Anti-HBe | 23        |
| Guangdong  | 265 Controls to PHC | H          | HBsAg 7, Anti-HBs, Anti-HBe | 5         |
| Ibid.      | 2443 Male prisoners | R          | HBsAg 25, Anti-HBs 46, Anti-HBe 81 | 24        |
| Guangxi    | 173 Controls to PHC | H          | HBsAg 16, Anti-HBs 12, Anti-HBe | 13        |
| Ibid.      | 1310 Adults | H          | HBsAg 13, Anti-HBs 9, Anti-HBe | 12        |
| Ibid.      | 35041 All ages | H          | HBsAg 13, Anti-HBs 8, Anti-HBe | 11        |
| Ibid.      | 40 Controls to PHC | R          | HBsAg 11, Anti-HBs 63, Anti-HBe 88 | 6         |
| Ibid.      | 49 Controls to PHC | R          | HBsAg 23, Anti-HBs 63, Anti-HBe 88 | 15        |
| Ibid.      | 11072 Adults | H          | HBsAg 17, Anti-HBs, Anti-HBe | 7         |
| Ibid.      | 304 Adults men | R          | HBsAg 22, Anti-HBs, Anti-HBe | 14        |
| Henan      | 1064 All ages | R          | HBsAg 26, Anti-HBs, Anti-HBe | 25        |
| Ibid.      | 579 Farmers* | R          | HBsAg 32, Anti-HBs 38, Anti-HBe 79 | 26        |
| Hunan      | 3089 All ages | RSH        | HBsAg 18, Anti-HBs 32, Anti-HBe 74 | 21        |
| Jiangsu    | 290 Factory workers | R          | HBsAg 9, Anti-HBs 53, Anti-HBe 72 | 18        |
| Liaoning   | 66 Factory workers | R          | HBsAg 8, Anti-HBs 39, Anti-HBe 48 | 18        |
| Shandong   | 926 Various | R          | HBsAg 5, Anti-HBs, Anti-HBe | 28        |
| Ibid.      | 1367 All inhabitants | H          | HBsAg 7, Anti-HBs, Anti-HBe | 29        |
| Ibid.      | 436 All inhabitants | H          | HBsAg 6, Anti-HBs 10, Anti-HBe 40 | 30        |
| Ibid.      | 107 Controls to PHC | H          | HBsAg 8, Anti-HBs 55, Anti-HBe 58 | 31        |
| Ibid.      | 977 Farmers | H          | HBsAg 9, Anti-HBs 19, Anti-HBe 72 | 32        |
| Ibid.      | 401 Clinical staff | R          | HBsAg 7, Anti-HBs 41, Anti-HBe 68 | 33        |
| Ibid.      | 426 Factory workers | R          | HBsAg 25, Anti-HBs 37, Anti-HBe 70 | Present study |
| Shanghai   | 4822 Adults | H          | HBsAg 10, Anti-HBs 9, Anti-HBe | 34        |
| Ibid.      | 365 All ages | R          | HBsAg 7, Anti-HBs 37, Anti-HBe 48 | 35        |
| Ibid.      | 520 Preschool children | R          | HBsAg 8, Anti-HBs 48, Anti-HBe 55 | 36        |
| Ibid.      | 290         | R          | HBsAg 8, Anti-HBs 48, Anti-HBe 65 | 18        |
| Shanxi     | 521 All ages | RSH        | HBsAg 8, Anti-HBs 23, Anti-HBe 39 | 37        |
| Ibid.      | 2122 All age* | R          | HBsAg 36, Anti-HBs 31, Anti-HBe 72 | 38        |
| Ibid.      | 429 Factory workers | R          | HBsAg 8, Anti-HBs 40, Anti-HBe 56 | 18        |
| Sichuan    | 428 Adult blood donors | H          | HBsAg 4, Anti-HBs 85, Anti-HBe | 39        |
| Zhejiang   | 5158 All ages | H          | HBsAg 13, Anti-HBs, Anti-HBe | 40        |

* Name of province, except for two cities of Beijing and Shanghai. * R for radioimmunoassay, and H for hemagglutination assay. + Overall rate of infection as defined by the rate of those positive to any of the 3 markers. * Not studied. * 1-10 year-old children, studied in 1979. 1-6 year-old children, studied in 1987. * Highly infected with HBV. * 316 hepatitis cases are included.
HBV Markers Among Yantai Workers

Table 4. HBsAg+ prevalence in Shandong Province by ages.

| Study Region          | No. of subjects | Age range | Reference |
|-----------------------|-----------------|-----------|-----------|
|                      |                 | 0 to 9    | 10 to 19  | 20 to 29  | 30 to 39  | 40 to 49  | 50 & over | All ages |
| Changxue County       | 926             | 3.2       | 3.4       | 4.3       | 5.9       | 10.5      | 6.6       | 5.4       |
| Huimin County         | 1367            | 4.5       | 6.4       | 12.2      | 8.0       | 11.8      | 1.8       | 6.5       |
| Jinan City            | 436             | 0.0       | 4.4       | 6.9       | 6.0       | 12.2      | 10.6      | 6.2       |
| Shandong Provincea,b  | 107             |           |           |           |           |           |           | 8.4       |
| Penglai Countya       | 977             |           | 26.3      | 29.5      | 18.3      | 14.3      | 19.0      | 25.4*     |
| Zibo City             | 401             |           |           |           |           |           |           | 7.2       |
| Yantai City           | 426             |           |           |           |           |           |           | 23.4*     |

* Significantly different from counterpart values (p<0.01).
a/ Break-down by age is not given. b/ Hospital patients from the Province. c/ Not studied.

Counterparts in other cities, indicating that HBV infection is endemic among this study population. In addition, the fact that the persistent carrier rate is almost 1.5-fold higher in younger people (those below 30 years of age) as compared with older people suggest that an unidentified episode might have happened in recent 10-20 years which provoked the increase in the HBV carrier rate. It would be more informative if the rates for younger inhabitants were available.

Several factors have been discussed in explaining the high HBsAg prevalence among various Chinese populations studied. For example, Luo et al.15) considered both vertical transmission from carrier mothers to their new-borne babies and close family contacts during the post-natal period as routes of HBV infection to produce persistent HBsAg carriers. Tang et al.42) examined HBV infection markers of 35 fetuses from HBsAg+ mothers after induced abortion in comparison with 10 fetuses from HBsAg- mothers, and observed that the sign of HBV infection was positive in sera of 7 cases in the former group (20%) in contrast to none in the latter. In the former group, 12 cases out of 27 liver tissues (44.4%) were positive to the infection when P-labeled HBV-DNA was employed as a probe, suggesting that intra-uterine infection is also an important mode of HBV transmission42). In this connection, it is worthy to note that Duan et al.43) in fact succeeded to interrupt mother-to-baby transmission of HBV by the administration of HBV vaccine to the babies born to HBsAg+ mothers. Regarding the latter possibility, Huan et al.50) observed in their epidemiological study of preschool children in Shanghai that the habit of premastication of food to feed children is associated with two-fold higher risk of the infection within a family. Opinions are equivocal among Chinese scientists on possible contribution of aflatoxin B contamination of food as a co-causative factor of PHC in combination with persistent HBV infection, in explaining high PHC incidence among Guangxi inhabitants13,14).

A few more reports are available in which trials were made to explain the mode of HBV infection among Chinese inhabitants outside the Continent. In Sin-
gapore, Quak et al. examined Chinese children for HBV infection in comparison with their counterparts of Malay and Indian origin and found that, although HbsAg+ prevalence appeared to be almost comparable among the 3 ethnic groups, the prevalence of anti-HBs and anti-HBc cases were significantly higher among Chinese children than in Malay or Indian children. In a study of babies born to HbsAg+ mothers in Taiwan, Stevens and others observed that the risk of babies to be HbsAg+ increased when his/her mother had high titer HbsAg, when the umbilical cord blood was HbsAg+, or when his/her sibling was HbsAg+, and concluded that the vertical transmission occurs rather frequently. In contrast, Lam et al. observed a sharp increase in HbsAg+ prevalence from first (less than 10%) toward fourth decade (over 40%) of life (and then decreases thereafter) among Chinese population in Hongkong, and thought that the dominant mode of HBV transmission among Chinese people was likely to be horizontal rather than vertical.

At the moment, no plausible explanation is available to understand the unusually high HBV infection prevalence among the population studied. Whether the prevalence is high in Yantai City in general or it is so among the study population only is still yet to be elucidated. Careful observation of the local culture and the way of daily life appears to be extremely important in order to identify the social habits which enhance the risk of infection at an early stage of life.

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