RESEARCH COMMUNICATION

# The Effects of the Hepatitis B Virus and Occupational and Lifestyle Factors on Liver Function Among Workers in Shanghai

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## Abstract

**The hepatitis B virus (HBV) infection is a major health problem in China. This study examined liver function in relation to HBV infection, and the occupational and lifestyle factors among workers in Shanghai. The study included 690 male workers aged 20-59 employed at a steel manufacturing company. The occupational and lifestyle factors were evaluated by self-administered questionnaire addressing worksite, exposure to dust or chemicals, history of cigarette smoking and habitual alcohol consumption. The prevalence of hepatitis B surface antigen(HBsAg) seropositivity was 21.4%. Elevated values of aspartate aminotransferase (AST, >30IU/liter) appeared in HBsAg-positive and current alcohol drinking groups but statistically on the borderline. There was a positive linear trend in the odds ratios(ORs) among age groups and ethanol consumption levels for elevated values of γ-glutamyl transferase (GGT, >50IU/liter). There was no clear association between occupational exposure and liver functions. When the effects of HBsAg and the current alcohol drinking status on the elevated value of AST were examined simultaneously, OR for cases with HBsAg-positive and current alcohol drinking rose to 2.85(95%CI .98-8.28) against reference cases with HBsAg-negative and non-alcohol drinking, although this association was statistically on the borderline. The results indicated that some interventional attempts including educational strategy for alcohol drinking would be important among the HBsAg-positive cases to reduce the risk of liver dysfunction and further, hepatocellular carcinoma.**

**Key words:** hepatitis B virus - aspartate aminotransferase - alcohol drinking - occupational exposure -China

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## Introduction

Chronic hepatitis B virus (HBV) infection is a common public health problem around the world, particularly in China and some Asian countries (Lee, 1997). More than half the population is infected at some time in their lives in those areas and nearly 10 percent are estimated to be chronic carriers of the virus (Gust, 1996; Malik and Lee, 2000). The problems of HBV infection among the carrier cases include developing cirrhosis or primary hepatocellular carcinoma (HCC). While the method for prevention of liver cirrhosis or HCC is primarily to prevent the development of HBV carriers caused by infection during infancy (Andre F, 2000), some aspects of its development are suspected to relate to non-viral factors; habitual alcohol drinking, cigarette smoking, and environmental and occupational exposures (Chen et al., 1997).

Since 1994, we have had a project to establish an effective program for the prevention of HCC and other liver diseases for a working population in the Shanghai area. Studies on HBV infection in China have mostly focused on the community (Yeh et al., 1989; Zhang et al., 1998), and little

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information on the status of liver dysfunction was available for the working population. This report describes the state of HBV infection and analyzes its effects when combined with occupational and lifestyle factors on liver function in a working population.

## Materials and Methods

The subjects of the study comprise a number of workers employed in a steel manufacturing company in the Baoshan district of Shanghai. The total number of employees is about 23,000. The results of annual health examinations indicated that diseases of the digestive system, gastric ulcers, liver cirrhosis, and malignant neoplasm in the stomach and liver were major health problems in this working population. Among those diseases, HCC was identified as the most serious and urgent to be prevented. The subjects of this study were 690 male workers belonging to the clerical and manufacturing sites who had health examination tests in their health checkups in the summer of 1995. These subjects completed the conventional liver function tests of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-gulutamyl- transferase (GGT). Serum markers of HBV and HCV infections, including hepatitis B surface antigen(HBsAg) and antibody(HBsAb), hepatitis C virus antibody(anti-HVC), and alpha-fetoprotein(AFP) were assayed using the EIA method(Dainabot, Tokyo, Japan). In this study, the upper normal limits for serum AST, ALT, and GGT values were 30, 40, and 50 IU/liter, respectively and for AFP, 10ng/ml.

Information on the working environment and lifestyle characteristics was obtained through a self-administered questionnaire at the time of the health examination. Details of the information include clerical or non-clerical work, exposure to dust or chemicals, birthplace, history of liver diseases, cigarette smoking, and alcohol consumption. For alcohol consumption, based on the number of bottles or cups consumed a day, daily ethanol intake was calculated by assuming the ethanol content in each bottle/cup to be 40% in whisky, 15% in wine or liquor, and 4% in beer.

Age-adjusted odds ratios (ORs) and their 95 percent confidence intervals (95%CIs) for potential risk factors relating to elevated values of AST, ALT, and GGT were estimated by the Cochran-Mantel-Haenszel method, using the SAS statistical package (SAS Institute, Inc., 1991).

## Results

Table 1-1 shows the age distribution and results of the serologic markers and liver function tests of the subjects. More than 75% of the subjects were over the age of 40. A positive rate of HBsAg accounted for 21.4% of the subjects,

**Table 1-1. Characteristics of the Subjects-age Distribution, Serologic Markers, and Liver Function Tests**

| Variable | n | % | Age Distribution(%) 20-39 | 40-49 | 50-59 | $\chi^2$ | p |
|---|---|---|---|---|---|---|---|
| Age(years) | | | | | | | |
| 20-39 | 172 | 24.9 | | | | | |
| 40-49 | 295 | 42.8 | | | | | |
| 50-59 | 223 | 32.3 | | | | | |
| HBsAg/HBsAb* | | | | | | | |
| -/- | 239 | 34.6 | 40.7 | 32.5 | 32.7 | | |
| -/+ | 303 | 43.9 | 40.7 | 45.4 | 44.4 | | |
| +/- | 139 | 20.1 | 18.0 | 20.7 | 21.1 | | |
| +/+ | 9 | 1.3 | .6 | 1.4 | 1.8 | 4.6 | .59 |
| anti-HCV* | | | | | | | |
| - | 682 | 98.8 | | | | | |
| + | 8 | 1.2 | | | | | |
| AFP level(ng/ml)* | | | | | | | |
| ≤10 | 682 | 98.8 | | | | | |
| >10 | 8 | 1.2 | | | | | |
| AST level(IU/l)* | | | | | | | |
| ≤30 | 657 | 95.2 | 96.5 | 94.6 | 95.1 | | |
| >30 | 33 | 4.8 | 3.5 | 5.4 | 4.9 | .91 | .63 |
| ALT level(IU/l)* | | | | | | | |
| ≤40 | 662 | 96.2 | 96.5 | 96.3 | 96.0 | | |
| >40 | 26 | 3.8 | 3.5 | 3.7 | 4.0 | .08 | .96 |
| GGT level(IU/l)* | | | | | | | |
| ≤50 | 645 | 93.5 | 97.7 | 92.5 | 91.5 | | |
| >50 | 45 | 6.5 | 2.3 | 7.5 | 8.5 | 6.9 | .03 |

* HBsAg, hepatitis B surface antigen; HBsAb, hepatitis B surface antibody; anti-HCV, hepatitis C virus antibody
AFP, α-fetoprotein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ-glutamyltransferase;
-, negative; +, positive

with anti-HCV only 1.2%. An elevated value of AFP was observed in 1.2 % of the subjects, and those of AST, ALT, and GGT accounted for 4.8, 3.8, and 6.5%, respectively. The age distribution of the positive rate of HBsAg and the percentage of elevated value of AST, ALT, and GGT was not statistically significant except for GGT; a greater percentage appearing in the older age groups.

Characteristics of the subjects including history of liver disease, birthplace, working environment, history of cigarette smoking and habitual alcohol drinking, and ethanol consumption are provided in Table 1-2. Twelve percent of the subjects reported history of liver diseases. Eighty six percent of the subjects were born in Shanghai and its surrounding areas. Non-clerical workers accounted for 79 percent of the subjects, and those who had occupational exposures to chemicals, dust, or solvents were 33%. Long-term cigarette smokers accounted for 66% of the subjects. When smoking habits were analyzed by smoking index, a value over 200 accounted for 40 percent of the subjects. Nearly 60 percent of the subjects were not alcohol drinkers, and a value of daily ethanol intake over 20ml accounted for 25% of the subjects. The significant differences of age distribution among these item strata were observed in worksite, occupational exposure, smoking index, and ethanol consumption. In general, the higher percentages of those who engaged in clerical works, were exposed to chemicals or dust, had a high smoking index, and a high ethanol consumption appeared in the older age groups.

Tables 2-1 and 2-2 show the odds ratios (ORs) of variables such as HBsAg-positive and those listed in tables 1-1 and 1-2 associated with elevated values of AST, ALT, and GGT. While marginal, the elevated level of AST was positively associated with HBsAg–positive (OR=1.92, 95%CI .98-3.75) and alcohol drinking (OR=1.85 95%CI .99-3.47), when HBsAg-negative and non-drinker were considered as reference values. The elevated value of GGT was positively associated with age and alcohol drinking. When ages 20-39 years were considered as reference values, the OR for an elevated value of GGT increased to 3.39(95%CI 1.15-9.99) for ages 40-49, and 3.91(95%CI 1.31-11.72) for ages 50-59. The linear trend of these associations was statistically significant(p=.02). With respect to alcohol drinking and ethanol consumption, the OR of current drinkers was 3.88(95%CI 2.06-7.32) against non-drinkers, and 2.35(95%CI .93-5.93) for under 20ml of daily ethanol intake, 4.84(95%CI 2.52-9.31) for over 20ml. The linear trend of

**Table 1-2. Characteristics of the Subjects-history of Liver Disease and Lifestyle Variables**

| | | | Age Distribution(%) | | | | |
|---|---|---|---|---|---|---|---|
| | n | % | 20-39 | 40-49 | 50-59 | $\chi^2$ | p |
| History of liver disease | | | | | | | |
| No | 609 | 88.4 | 86.6 | 87.1 | 91.5 | | |
| Yes | 80 | 11.6 | 13.5 | 12.9 | 8.5 | 3.1 | .21 |
| Birthplace | | | | | | | |
| Shanghai area | 593 | 86.2 | 86.1 | 87.7 | 84.3 | | |
| Others | 95 | 13.8 | 14.0 | 12.3 | 15.7 | 1.2 | .54 |
| Worksite | | | | | | | |
| Clerical | 145 | 21.2 | 14.6 | 18.8 | 29.4 | | |
| Non-clerical | 539 | 78.8 | 85.4 | 81.2 | 70.6 | 14.3 | .00 |
| Occupational exposure⌘ | | | | | | | |
| No | 464 | 67.3 | 78.5 | 63.3 | 64.1 | | |
| Yes | 225 | 32.7 | 21.5 | 36.7 | 35.9 | 13.0 | .00 |
| Cigarette smoking | | | | | | | |
| No | 231 | 33.5 | 32.8 | 31.2 | 37.2 | | |
| Yes | 435 | 63.1 | 65.5 | 65.8 | 57.9 | | |
| Quit | 23 | 3.3 | 1.8 | 3.1 | 4.9 | 5.9 | .20 |
| Smoking index● | | | | | | | |
| 0 | 231 | 33.6 | 32.9 | 31.3 | 37.2 | | |
| -200 | 180 | 26.2 | 51.2 | 21.8 | 13.0 | | |
| 200- | 276 | 40.2 | 15.3 | 46.9 | 49.8 | 92.3 | .00 |
| Alcohol drinking | | | | | | | |
| No ♦ | 411 | 59.6 | 65.1 | 55.6 | 60.5 | | |
| Yes | 279 | 40.4 | 34.9 | 44.4 | 39.5 | 4.2 | .12 |
| Ethanol consumption (ml/day) | | | | | | | |
| 0 | 411 | 59.6 | 65.1 | 55.6 | 60.5 | | |
| -20 | 104 | 15.1 | 19.2 | 14.5 | 12.6 | | |
| 20- | 175 | 25.4 | 15.7 | 29.8 | 26.9 | 13.5 | .01 |

⌘ Exposure to dust or chemicals
● cigarettes/day x years
♦ including ex-drinkers

these associations were statistically significant (p=.00). No of significant association was observed between elevated level of ALT and potential risk factors.

While statistical significance is marginal, both HBsAg-positive and alcohol drinking might be related to an elevated value of AST. We then assessed the interaction of combinations of hepatitis B virus infection and alcohol drinking status (Table 3). When HBsAg-negative and no alcohol drinking was a reference value, ORs increased with the combination of HBsAg and alcohol drinking status; HBsAg-negative and active alcohol drinking (OR=1.81, 95%CI .78-4.23), HBsAg-positive and no alcohol drinking (OR=2.29, 95%CI .83-6.33) and HBsAg-positive and active alcohol drinking (OR=2.85, 95%CI, .98-8.28). Though no statistical significance of ORs among each category was observed, there was a significant linear trend of ORs in these associations(p=.03).

## Discussion

This study showed that a positive rate of HBsAg accounted for 21%, but anti-HCV was only 1% of the study population. When these values are compared with similar studies of factory workers in industrialized cities in China (Seiji K et al., 1991; Seiji K et al., 1991), there was no great difference except for HCV, where no data was available from previous studies. Our sample was comprised of a limited section of the working site and covered only 3% of the total workers of a huge steel company wishing to have health examinations. This may have caused sampling bias in our study.

Our data indicate that HBV infection, not HCV, is a major burden to liver disease in this population. There was, however, no great influence of HBsAg-positive on liver function in spite of a high prevalence of HBV infection. Only elevated values of AST showed a positive association with HBsAg status. Variables relating to a positive association with liver function other than HBV infection were limited to age, current status of alcohol drinking and amount of ethanol consumption for GGT, birthplace and alcohol drinking for AST, while the associations with AST were statistically on the borderline.

Among the studies on the association between HBV and HCV infection and liver function, HBsAg-positive proved to play a minor (Une et al., 1994) and anti-HCV a major role on ALT or AST levels (Wang et al., 1998; Chang et al., 2000). An unclear relation between HBV infection and liver function might be due to the clinical stage of HBV infection. Our HBsAg-positive cases seemed to be asymptomatic ones, while there was no continuous identification of HBV infection and no examination of HBe antigen or antibody status in the study population.

Studies on HBV or HCV infection have been concerned mainly with the development of a fatty liver, liver cirrhosis, and HCC. They have revealed that a HBV or HCV infection is an important causative factor in chronic liver diseases and

**Table 2-1. Odds Ratios(ORs) for Elevated Values of AST*, ALT*, and GGT*-HBV Infection, Birthplace, and Working Situations**

| | AST* | | | ALT* | | | GGT* | | |
|---|---|---|---|---|---|---|---|---|---|
| | OR❖ | 95%CI♦ | p | OR❖ | 95%CI♦ | p | OR❖ | 95%CI♦ | p |
| Age(years) | | | | | | | | | |
| 20-39 | 1.00 | | | 1.00 | | | 1.00 | | |
| 40-49 | 1.62 | 0.67-3.94 | .28 | 1.07 | 0.39-2.94 | .90 | 3.39 | 1.15-9.99 | .02 |
| 50-59 | 1.82 | 0.73-4.53 | .19 | 1.16 | 0.40-3.31 | .79 | 3.91 | 1.31-11.72 | .01 |
| | | | | | | | | p for trend= | .02 |
| HBsAg■ | | | | | | | | | |
| - | 1.00 | | | 1.00 | | | 1.00 | | |
| + | 1.92 | 0.98-3.75 | .05 | 1.10 | 0.43-2.79 | .84 | 0.87 | 0.40-1.87 | .73 |
| History of liver disease | | | | | | | | | |
| No | 1.00 | | | 1.00 | | | 1.00 | | |
| Yes | 1.57 | 0.67-3.67 | .29 | 1.40 | 0.47-4.17 | .54 | 1.52 | 0.66-3.51 | .32 |
| Birthplace | | | | | | | | | |
| Shanghai area | 1.00 | | | 1.00 | | | 1.00 | | |
| Others | 0.29 | 0.08-1.15 | .08 | 0.80 | 0.24-2.71 | .72 | 1.19 | 0.51-2.78 | .69 |
| Worksite | | | | | | | | | |
| Clerical | 1.00 | | | 1.00 | | | 1.00 | | |
| Non-clerical | 1.47 | 0.63-3.41 | .37 | 1.55 | 0.52-4.56 | .43 | 1.05 | 0.50-2.21 | .91 |
| Occupational⌘ exposure | | | | | | | | | |
| No | 1.00 | | | 1.00 | | | 1.00 | | |
| Yes | 0.76 | 0.38-1.54 | .45 | 0.91 | 0.39-2.09 | .82 | 1.03 | 0.54-1.96 | .94 |

* AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ-gulutamyltransferase

❖ ORs are age-adjusted only for the variables showing a significant difference in age distribution

♦ confidence interval, ■hepatitis B surface antigen, -, negative; +, positive, ⌘exposure to dust or chemicals

HCC, but the degree of its importance varied among the studies. Some studies (Chuang et al., 1992; Lee et al., 1992; Tsai et al., 1996; Tsai et al., 1997; Zhang et al., 1998) identified that HBV and/or HCV infection were independent or additional effect modifications of HCC development, while others(Leung et al., 1992; Ito et al., 1993; Okuno et al., 1994) saw them as insignificant aetiological factors or of minor epidemiological significance for HCC.

As shown in table 3, the combined effect of HBsAg and alcohol drinking status on elevated AST had a weak positive association, but statistically on the borderline. When the effects of HBV and/or HCV infection on liver function were considered in combination with lifestyle factors, HCV infection and a high body mass index were predominant factors in elevated serum ALT levels (Une, et al., 1994), but alcohol drinking was a minor factor in this population. Another study of Japanese cases indicated that alcohol consumption and concomitant HCV infection apparently facilitated the development of hepatitis (Ohta, Watanabe, and Nakajima, 1998).

For the development of HCC or liver cirrhosis, alcohol drinking and cigarette smoking seemed to have independent or sometimes synergistic effects, where HBV or HCV infection played the greatest role in these conditions (Chen et al. 1991, Hsing et al., 1991;Yu et al., 1997). There was significant interaction on an additive scale for the risk of HCC development between high-titer anti-HCV status and a history of smoking in the Japanese community population(Mori et al., 2000). While our study does not include anthropometric data, and considered only smoking and drinking status as lifestyle factors, further studies will be required to investigate other promising sources relating to liver function profiles.

There was no clear association between occupational factors and liver function. Due to limited information on working conditions, occupational exposure was available only for chemicals and dust. Chen et al(1991) reported that GGT activity increased independently among paint-manufacturing workers with direct exposure to solvent mixtures. In our analysis, there was no information on the severity of exposure and, as appeared in Table 2-1, there was no statistical difference of odds ratio between the binary response to occupational exposure when chemicals and dust were combined. An elevated value of AFP accounted for only 1.2% of the study population. While no information was available for the clinical stage of HBV infection, this implied no direct association between HBsAg-positive and AFP level as reported in the Taiwanese population (Lee HL, Chung YH, and Kim CY, 1991; Tsai et al., 1994).

The primary sources of spreading HBV infection have been considered as both prenatal and horizontal HBV transmission from HBV carrier mothers to newborns. To prevent early infection, a mass vaccination program has proved to be effective (Chen, et al., 1996; Zhao, Xu, and Lu, 2000; Lin et al., 1998), but incomplete (Tang et al., 1998), to control HBV infection in many hyperendemic areas. An immunization program, however, will cost a lot of money and will be time-consuming. The attitude towards for vaccine acceptance, vaccination coverage, and better training in counseling for village doctors will be the key to success for this preventive method (Clayton et al., 1993; Wang et al., 1998).

In summary, there were no severe cases of liver dysfunction among the study population in spite of a high prevalence of HBV infection. The results indicated that some interventional steps including health educational strategy for

**Table 2-2. Odds Ratios(ORs) for Elevated Values of AST*, ALT*, and GGT*-Cigarette Smoking and Alcohol Drinking**

| | AST* | | | ALT* | | | GGT* | | |
|---|---|---|---|---|---|---|---|---|---|
| | OR | 95%CI❖ | p | OR | 95%CI❖ | p | OR | 95%CI❖ | p |
| Cigarette smoking | | | | | | | | | |
| No | 1.00 | | | 1.00 | | | 1.00 | | |
| Yes | 1.00 | 0.52-1.96 | .98 | 0.59 | 0.24-1.47 | .26 | 1.18 | 0.60-2.31 | .64 |
| Smoking index♦ | | | | | | | | | |
| 0 | 1.00 | | | 1.00 | | | 1.00 | | |
| -200 | 1.53 | 0.64-3.65 | .34 | 1.07 | 0.38-2.99 | | 0.58 | 0.20-1.66 | .31 |
| 200- | 0.80 | 0.36-1.82 | .61 | 0.63 | 0.26-1.57 | | 1.22 | 0.62-2.39 | .57 |
| Alcohol drinking | | | | | | | | | |
| No⌘ | 1.00 | | | 1.00 | | | 1.00 | | |
| Yes | 1.85 | 0.99-3.47 | .05 | 1.28 | 0.57-2.87 | .55 | 3.88 | 2.06-7.32 | .00 |
| Ethanol consumption (ml/day) | | | | | | | | | |
| 0 | 1.00 | | | 1.00 | | | 1.00 | | |
| -20 | 1.25 | 0.44-3.52 | .68 | 1.38 | 0.49-3.88 | .54 | 2.35 | 0.93-5.93 | .07 |
| 20- | 1.79 | 0.82-3.89 | .14 | 1.28 | 0.48-3.33 | .62 | 4.84 | 2.52-9.31 | .00 |
| | | | | | | | | p for trend = | .00 |

* AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ-gulutamyltransferase
ORs are age-adjusted only for the variables showing a significant difference in age distribution
❖ confidence interval, ♦ cigarettes/day x years, ⌘ include quit drinking

**Table 3. An Assessment of the Combined Effects of HBsAg and Alcohol Drinking Status on Elevated Values of AST**

| HBsAg/alcohol drinking | no. of subject AST≤ 30 | AST > 30 | OR | 95%CI | p |
|---|---|---|---|---|---|
| Negative/no | 313 | 10 | 1.00 | - | - |
| Negative/yes | 207 | 12 | 1.81 | 0.78-4.23 | .17 |
| Positive/no | 82 | 6 | 2.29 | 0.83-6.33 | .11 |
| Positive/yes | 55 | 5 | 2.85 | 0.98-8.28 | .06 |
| | | | | p for trend= | .03 |

HBsAg, hepatitis B surface antigen; AST, aspartate aminotransferase
OR, odds ratio; CI, confidence interval

alcohol drinking will be important to reduce the risk of liver dysfunction and HCC among HBsAg-positive cases, while the association was found only in AST levels and statistically on the borderline. Further studies with periodical follow-up of clinical examinations will be required for early detection of liver diseases in this working population.

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