PREVALENCE OF HEPATITIS B AND C VIRUS INFECTION AMONG WOMEN IN JEJU ISLAND, REPUBLIC OF KOREA

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Abstract. Hepatitis B and C virus infection prevalence was investigated in the Island of Jeju (formerly Cheju), the Republic of Korea, by means of a small-scale sero-epidemiological survey in 2000. Adult women in the city of Jeju (the provincial capital) and two fishing-farming villages A and B were invited to offer venous blood samples for immunological examination for infection markers of two virus and serum biochemistry for liver function. In practice, 66 married women (33, 16 and 17 women from the city, Village A and Village B, respectively) volunteered. Sera were separated on site and were assayed for HBsAg, anti-HBs, anti-HBc, and anti-HCV positivities and liver function markers including AST, ALT and γ-GTP. The serum assay showed that the prevalence of $HbsAg^+$ or anti-HCV^+ cases was low (5 and 2%, respectively), whereas that of anti-HBs^+ and anti-HBc^+ cases were high (71 and 62%) so that the over-all HBV positivity was 82%. There were essentially no urban-rural difference or age-dependent changes in the positivity. Comparison with the prevalence reported in literature shows that prevalence of $HBsAg^+$ and anti-HCV^+ is in general agreement with the values reported for the populations in general, but HBV^+ prevalence might be somewhat higher than the levels reported for the general populations.

INTRODUCTION

Endemicity of hepatitis B and C virus (to be abbreviated as HBV and HCV, respectively) is a focus of interest of cancer epidemiologists because infection with these viruses early in life is a risk factor of hepatocellular carcinoma at the later stage (*eg* International Agency for Research on Cancer, 1994). With regard to HBV infection in Republic of Korea in particular, Ahn (1996) for example summarized in a review that the HBV infection prevalence is about 44% among the general population in the Republic of Korea, and, based on clinical records in Seoul National Hospital, pointed out that a high incidence of HBV infection is associated with liver diseases such as chronic active hepatitis, liver cirrhosis or hepatocellular carcinoma.

The Island of Jeju (with a population of $53x10^4$ people in a space of 1,845 km^2), the main island in Jeju Province, the Republic of Korea, is geographically unique in the Republic in the sense that the island is separated from other parts of the peninsula by a straight so that traffic from outside is only via air or sea, and that population is less dense (287 people/km^2 in comparison with >400 people/km^2 for the whole country).

Being interested to know if such geographical conditions may affect infection epidemiology of HBV and HCV, this study group has recently conducted a small-scale pilot survey, because only one report (limited

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to HBV infection) has been published in literature (Moon and Youn, 1997) on hepatic virus infection among Jeju poplation. The results of the study are presented in this report in comparison with the results on the main part of the Republic reported in the literature (Koo *et al*, 1984; Lee *et al*, 1984; Choi, 1986; Park, 1987; Ryoo *et al*, 1987; Yoo *et al*, 1988, 1991; Park *et al*, 1991; Ahn *et al*, 1992; Kim *et al*, 1990; 1992, 1993, 1995a,b; Han *et al*, 1994; Youn, 1994; Joo *et al*, 1999).

MATERIALS AND METHODS

Study population and design

A seroepidemiological survey on HBV and HCV infection was conducted in Jeju Island, off shore the south-west coast of Korean penninsula late in October 2000. As the survey size was expected to be small, only adult people of one sex (women) were selected to avoid possible confounding effects sex and age on infection prevalence (Ahn *et al*, 1992; Kim *et al*, 1992). In practice, house-wives in the city of Jeju (the provincial capital with a population of 270,842 people), a fishing-farming village some 20 km east-north-east of the city (Village A with 1,576 residents) on the north coast of the island, and another fishing-farming village some 40 km south-west (Village B with 2,600 inhabitants) on the south coast were invited to participate in the study by offering blood samples.

In practice, 33, 16 and 17 women in the city, Village A and Village B, respectively, volunteered (the city, Village A and Village B group, respectively). They were 43.5 years of age on an average (range; 29 to 54 years) with no significant ($p>0.05$) difference among the three survey sites (Table 1). Blood samples were drawn from cubital vein late in the morning (with no breakfast). In addition, the participants had a medical interview on history of major diseases, current social habits of smoking and alcohol intake, and marital status (all married).

Table 1
Age distribution of the participants by place of residence.

Place of residence	Number of women	Age (years)	
		AM±ASD	Range
City	33	43.5±6.3	34 - 54
Village A	16	43.2±8.4	29 - 54
Village B	17	43.6±7.6	29 – 53
Total	66	43.5±7.1	29 - 54

Assay for markers of hepatitis virus B and C infection, and liver function

Serum was separated on-site by centrifugation, and kept frozen until analyzed in a clinical laboratory. HBV infection markers were assayed with RIA kits; HBV surface antigen (HBsAg) by AUSRIA® II-125, HBV surface antibody (anti-HBs) by AUSAB®, and HBV core antibody (anti-HBc) by RIA KIT® (all from Abbott-Dianabot, Tokyo, Japan). The assay for HCV antibody (anti-HCV) was by Ortho HCVab IRMA III (from Ortho-Clinical Diagnostics, Tokyo, Japan). The three serum enzymes of aspartate aminotransferase (ASAT: EC 2.6.1.1.), alanine aminotransferase (ALAT: EC 2.6.1.2.),γ-glutamyl transpeptidase (γ-GTP: EC 2.3.2.1.) were assayed by conventional methods. Criteria for evaluation of the immunological and enzymic assay results are summarized in Table 2. Borderline cases were taken as positive in dichotomous classification.

Statistical analysis

The distribution of serum enzyme activities was assumed to be log-normal rather than normal, and accordingly geometric means (GMs) together with geometric standard deviations (GSDs) were calculated. A normal distribution was assumed for ages. Chi-square test and unpaired *t*-test (after logarithmic conversion for enzymic assay results) were employed for detection of difference in prevalence and means, respectively. A probability of 0.05 was taken as a point for judgment of significance, considering relatively small numbers of the cases.

Table 2
Criteria for hepatitis B and C virus infection markers and serum enzymes

Examination		Criteria		
Item	Unit	Negative	Borderline	Positive
Hepatitis B infection marker				
HBsAg	Cut-off ratio	<1	≥1 to <5	≥5
Anti-HBs	Cut-off ratio	<1	≥1 to <2	≥2
Anti-HBc	Suppression	<30%	≥30% to <70%	≥70%
Hepatitis C infection marker				
Anti-HCV	Cut-off index	<1	-	≥1
Serum enzyme activity				
ASAT	IU/l	10-40[a]		
ALAT	IU/l	5-50[a]		
γ-GTP	IU/l	0-30[a]		

Abbreviations are: HBsAg, HBV surface antigen; anti-HBs, HBV surface antibody; anti-HBc, HBV core antibody; anti-HCV, HCV antibody; ASAT, aspartate aminotransferase (EC 2.6.1.1); ALAT, alanine aminotransferase (EC 2.6.1.2); γ-GTP, γ-glutamyl transpeptidase (EC 2.3.2.1).
[a] A normal range in the laboratory.

RESULTS

Possible difference in prevalence of HBV and HC infection

The positivity to three markers of hepatitis B virus infection (*ie* $HbsAg^+$, $anti\text{-}HBs^+$, and $anti\text{-}HBc^+$) and one hepatitis C virus infection marker ($anti\text{-}HCV^+$) was calculated for each place of residence (*ie*, survey site) (Table 3). With regard to HBV infection markers, $HbsAg^+$ prevalence was generally low in the three sites (0 to 18%), but the prevalence in Village B was significantly higher ($p<0.05$) than the rates in other two sites. In contrast, $anti\text{-}HBs^+$ and $anti\text{-}HBc^+$ prevalence was 50% or even higher throughout the three sites so that HBV^+ was as high as 63 to 88%. The HBV^+ prevalence for Village B (88%) tended to be higher than the rate for Village A (63%), although the difference was statistically insignificant ($p>0.05$). HVC infection prevalence was generally low in the three sites. Thus the rate was 0% in the City and Village A, and 6% in Village B without significant difference ($p>0.05$) among them.

Urban-rural comparison showed no significant difference ($p>0.05$) either in the prevalence of the three HBV infection markers (and therefore HBV^+ cases) or in $anti\text{-}HCV^+$ prevalence between the City group and a combination of Village A and Village B groups. Accordingly, cases in the three sites were combined, and further classified into two age groups of similar sizes to examine possible age-dependent differences in the prevalence. The comparison of the two age groups, *ie*, 34 women of 45 or less years of ages and 32 women of 46 or more years, failed to show any age-dependent difference in prevalence of the positivity to three HBV infection markers, HBV^+ prevalence or $anti\text{-}HCV^+$ prevalence ($p>0.05$ for all cases).

Accordingly, the over-all prevalence was calculated by combining all cases regardless of place of residence or ages (the 'total' column in Table 3). The prevalence was such that the rate was low both for $HbsAg^+$ and $anti\text{-}HCV^+$ cases (*ie*, 5% and 2%, respectively), whereas HBV^+ prevalence was well in excess of 80%. This high HBV^+ prevalence was primarily due to high rate for $anti\text{-}HBs^+$ (>70%) and $anti\text{-}HBc^+$ (>60%).

Table 3
Prevalence of hepatitis B and C virus infection markers by place of residence and by age group.

Indicative of hepatitis virus infection	Place of residence				Age group (years)		Total
	City	Village A	Village B	Vil. A+B	29-45	46-54	
Total No.	33	16	17	33	34	32	66
Hepatitis B							
$HBsAg^+$	0 (0%)	0 (0%)	3 (18%)	3 (9%)	2 (6%)	1 (3%)	3 (5%)
Anti-HBs^+	27 (82%)	9 (56%)	11 (65%)	20 (61%)	24 (71%)	23 (72%)	47 (71%)
Anti-HBc^+	18 (55%)	9 (56%)	14 (82%)	23 (70%)	19 (56%)	22 (69%)	41 (62%)
HBV^+	29 (88%)	10 (63%)	15 (88%)	25 (76%)	26 (76%)	28 (88%)	54 (82%)
Hepatitis C							
Anti-HCV^+	0 (0%)	0 (0%)	1 (6%)	1 (3%)	0 (0%)	1 (3%)	1 (2%)

Abbreviations are as under Table 2.
Values are the number of positive cases (percentages in parentheses). There is no significant ($p>0.05$ by chi-square test) difference in the prevalence among three sites except that $HBsAg^+$ prevalence was significantly ($p<0.05$) higher in Village B than in the City or in Village A. Urban-rural (*ie*, the City *versus* Villages A+B) difference is insignificant ($p>0.05$ for all markers). Differences between the two age groups are also insignificant ($p>0.05$).

Lack of evidence for liver dysfunction

In order to examine if HBV or HCV infection affected liver function of the subjects at the time of the survey, all subjects in combination were classified into two groups in terms of the infection, *ie*, 54 women who were positive either to HBV or to anti-HCV (in practice, the only woman who was anti-HCV^+ was also HBV^+) and 12 women who were negative to both HBV and to anti-HCV. The comparison on activities of ASAT, ALAT and γ-GTP between the two groups showed that, whereas the GM (GSD) for ASAT tended to be higher ($0.01<p<0.05$) in the positive group [16.7 IU/l (1.29)] than in the negative group [14.2 IU/l (1.29)], none in the both groups had ASAT higher than the upper normal limit of 40 IU/l. ALAT did not differ ($p>0.10$) between the two groups [12.7 IU/l (1.51) for the positive group and 12.3 IU/l (1.38) for the negative group], and such was also the case for γ-GTP [12.9 IU/l (1.53) and 11.8 IU/l (1.31), respectively]. When examined individually, ALAT was normal in all women irrespective of positivity to HBV or HCV infection. In case of γ-GTP, two women (47 and 52 years of age, both being no alcohol drinkers) were either $HbsAg^+$ or anti-HBc^+ in the order, and showed very moderate elevation in γ-GTP (38 and 41 IU/l, respectively). Their ASAT (13 and 24 IU/l) and ALAT (19 and 25 IU/l) however stayed normal, suggesting the absence of serious changes in liver function.

DISCUSSION

In order to evaluate the present observations in comparison with the prevalence reported for other part of the Republic, a literature survey was conducted for HBV and HCV prevalence; the results are summarized in Table 4. It is clear that most of published reports dealt with urban populations such as in the city of Seoul (the capital) (*eg*, Yoo *et al*, 1988; Kim *et al*, 1990, 1992; Park *et al*, 1991; Joo *et al*, 1999), Taegu (Park 1987), Ulsan (Kim *et al*, 1993), Kwangju (Han *et al*, 1994) or Pusan (Kim *et al*, 1995b). Two exceptions were the report by Choi (1986) and Moon and Youn (1997); the former studied HbsAg positivities among children (including young adults) in rural areas and the latter studied the population in Jeju island. The

Table 4
HBV and HCV infection prevalence among Korean populations reported in literature.

Reference	Prevalence(%)					Remark
	HBsAg$^+$	Anti-HBs$^+$	Anti-HBc$^+$	HBV$^+$	Anti-HCV$^+$	
Present study	4.5	71.2	62.1	81.8	1.5	Women in Jeju Island
Koo *et al*, 1984	7.1					Mothers (Seoul)
Lee *et al*, 1984	3.6					Mothers (Ko Sin Hosp)
Choi, 1986	12.6					15-17 year-olds (Rural)
Park, 1987	6.8	35.8	45.5	49.1		Med. students (Taegu)
Ryoo *et al*, 1987	8.5					Pregnants (Mokpo)
Yoo *et al*, 1988	11.7	65.2	78.8	84.7		Adult men (Seoul)
Yoo *et al*, 1988	9.5	45.6	50.9	61.2		Adult women (Seoul)
Kim *et al*, 1990					1.2	Blood donors (Seoul)
Park *et al*, 1991					1.3	Blood donors (Seoul)
Yoo *et al*, 1991	4.6			21.8		1985-1987 values[a]
Ahn *et al*, 1992	8.0			61.3		Review for '90s, men[a]
Ahn *et al*, 1992	6.1			52.8		Review for '90s, women[a]
Kim *et al*, 1992	6.5				1.7	Men (Seoul)
Kim *et al*, 1992	5.2				1.7	Women (Seoul)
Kim *et al*, 1993					0.6	Blood donors (Ulsan)
Han *et al*, 1994	5.0				0.9	Adults (Kwangju)
Yoon *et al*, 1994					1.8	Adults (Seoul)
Kim *et al*, 1995a	5.8	32.7			1.3	Adults (Chunan)
Kim *et al*, 1995b	7.4				3.0	Adults (Pusan)
Moon and Youn, 1997	10.0	49.3				Adult men (Jeju)
Moon and Youn, 1997	5.1	42.0				Adult women (Jeju)
Joo *et al*, 1999	12.0	87.9	80.0	89.4		Adult men (Seoul)
Joo *et al*, 1999	9.2	87.0	76.1	84.6		Adult women (Seoul)

Abbreviations are as under Table 2.
[a] Value covering the Republic of Korea as a whole.

population studied by Yoo *et al* (1991) is the beneficiary of a large-scale medical insurance system (about 0.4 million men in the whole country) that should cover both urban and rural people. Comparing the present observation with the values reported in literature, it appears likely that the HbsAg$^+$ prevalence for Jeju (4.5%) is no higher than other values, when the difference in the time of survey is not considered. In contrast, HBV$^+$ prevalence was substantially higher in Jeju (82%) than in other areas [mostly 26 to 61%, with two exceptions of 85% as reported by Yoo *et al* (1988) and Joo *et al* (1999)].

The report by Moon and Youn (1997) may deserve special attention because the report deals with people in Jeju, the target population of the present study. In their study, a substantial difference in HbsAg$^+$ prevalence was reported between two sexes, being higher in men (10%) than in women (5%). Whereas the prevalence rate for women (5.1%) was very close to the present observation (4.5%), the reported higher rate for men (10%) suggested that the overall prevalence for general population (*ie* men and women in combination) may be higher than the prevalence obtained in the present study on women. Unfortunately, values were not available for HBV$^+$ and anti-HCV$^+$, in the report of Moon and Youn (1997), and therefore no comparison is possible.

Chronological observation of trends in HbsAg$^+$ prevalence suggests that the prevalence had been higher (*eg*, >10%) both in urban

(Yoo *et al*, 1988) and rural areas (Choi, 1986) in the past than in later years [*eg*, 6% (Kim *et al*, 1992, 1995a,b)]. By analogy, it might be the case that the HBV infection rate in Jeju Island was higher in the past (*eg*, in the 1980s) than in recent years, and present high anti-HBs^+ (71%; Table 3) or anti-HBc^+ prevalence is a refection of the past high endemicity (*eg*, Ahn, 1996; Ahn *et al*, 1992). In this connection, it may be relevant to note that, since 1984 (national statistics being available from 1989 on), a nation-wide program of general population vaccination (*ie*, both children and adults) has been in practice in Korea (Ministry of Health and Welfare, 1999) including Jeju Province, as recommended by the World Health Organization (Kane, 1996) as well as in Korea (*eg*, Ahn, 1996). According to the report by Park *et al* (1994) on the population in the city of Ulsan, the vaccination rate among the population was 37%, being higher among teenagers (57%), and better educated people (*eg*, 46% among college graduates) In support of the efforts, successful results in reducing risk of primary liver cancer by vaccination have been reported (Lee *et al*, 1998).

With regard to HCV infection, less than ten reports are available on anti-HCV^+ prevalence (Table 4). Nevertheless, the reported prevalence rakes are generally low and below 2% except for 3% reported for Pusan (Kim *et al*, 1955b), suggesting that HCV infection is not a serious public health issue, not only in Jeju but in the Republic as a whole.

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