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Original Article

Prevalence of Hepatitis B Infection in the Southeastern Region of Turkey: Comparison of Risk Factors for HBV Infection in Rural and Urban Areas

Dursun Mehmet, Ertem Meliksah[1]*, Yilmaz Serif, Saka Gunay[1],
Özekinci Tuncer[2] and Simsek Zeynep[3]

Department of Gastroenterology, [1]Department of Public Health and [2]Department of Microbiology, Medical School of Dicle University, 21280 Diyarbakir and [3]Department of Public Health, Medical School of Harran University, Sanliurfa, Turkey

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SUMMARY: Although hepatitis B has been well studied, there are still aspects of its epidemiology that remain to be clarified. There are many regions with high seroprevalence, particularly in the developing regions of the world, and these regions are known to have different epidemiologic patterns. Nonetheless, there are currently no data on the differences in hepatitis B seroprevalence between urban and rural areas of Turkey. In the present study, therefore, we used 30-cluster sampling to determine and compare the prevalence of hepatitis B in the urban and rural areas of the least developed region of Turkey, the southeastern region. From 2,888 adults living in the region, blood samples were obtained from house visits, and screened for HBsAg, anti-HBs, and anti-HBcIgG. Factors associated with hepatitis B seroprevalence, particularly living in rural areas, were analyzed with multivariate methods. The seroprevalence of HBsAg was 8.2% in the rural and 6.2% in the urban areas. There was a statistically significant difference between urban and rural regions in terms of HBsAg positivity (crude OR: 0.74; 95% CI: 0.55 - 0.98). Exposure to hepatitis B virus (HBV) increased with age both in urban and rural areas. Lower education level was also an important risk factor for hepatitis B seropositivity in urban areas (adjusted OR: 1.66; 95% CI: 1.26 - 2.19) but not in rural ones (adjusted OR: 0.77; 95% CI: 0.36 - 1.69). Familial jaundice history was a statistically significant risk factor for HBsAg positivity in rural areas (adjusted OR: 2.15; 95% CI: 1.30 - 3.56) but not in urban ones (adjusted OR: 1.48; 95% CI: 0.96 - 2.27). This study shows that the prevalence of HBV infection in the southeastern region of Turkey is intermediate among the levels reported for the European region of the World Health Orgnization.

INTRODUCTION

Globally, the frequency of hepatitis B virus (HBV) infection is a function of various risk factors, and appears to be higher among males than females, among children than adults and among urban than rural communities (1). In Poland, the incidence of hepatitis B per 100,000 individuals was higher in urban (7.0) than in rural (4.9) populations (2), and in Spain the prevalence of hepatitis B and C markers was higher in individuals living in urban areas (3). In China, it was reported that no substantial difference was seen between the rural and urban populations (4). In developing countries, however, rural areas seem to have a higher risk than urban ones. For example, in Madagascar, a large difference in HBsAg prevalence was observed between urban (5.3%) and rural areas (26.0%) (5). An outbreak was reported in rural India, which was epidemiologically linked to the use of inadequately sterilized needles and syringes by unqualified medical practitioners (6). In the Asia-Pacific Region, the prevalence of HBV infection is consistently higher in rural than in urban areas and several common sources of infection, including iatrogenic and sexual transmission, have been implicated (7). The reports mentioned above are the evidence of an urban-rural difference in the epidemiologic pattern of HBV in different parts of the world. Risk factors for HBV infection may be different in urban areas and in rural areas. The strategies for the control of HBV infection should account for these differences.

Turkey is one of the countries with intermediate endemicity in the European region of the World Health Organization (WHO) (1). In this article, we aimed to determine differences in the prevalence of hepatitis B between rural and urban areas in the southeastern region of Turkey, which is an endemic area for malaria. In the study, risk factors for hepatitis B infection in the rural areas were compared with those in the urban areas. This is the largest serosurvey of hepatitis B yet performed in Turkey.

METHODS

Study area: The southeastern region, where the study was conducted, is the least developed region of Turkey in terms of economic, social, and health indices. Insufficient health services and lack of public awareness of health-related issues have increased the prevalence of diseases, particularly communicable diseases. The total population of the region under consideation is 6,604,000, and 40% of the population lives in rural areas (8).

Study population: Four of the nine provinces of the southeastern region (Diyarbakir, Sanliurfa, Batman, and Mardin) were randomly selected as the cities in which the study was to be conducted. The estimated HBsAg prevalence was 8%, and the sample size was calculated by using EpiInfo 2000 (9). Thus, the minimum sample size was calculated as 706, and taking into account the possible losses during data

*Corresponding author: Mailing address: Department of Public Health, School of Medicine, Dicle University, 21280 Diyarbakir, Turkey. Tel/Fax: +90-412-2488432, E-mail: mertem@dicle.edu.tr

collection and survey, we decided to collect 750 blood samples in each province (3,000 total). The 30-cluster sampling method, which is recommended by the WHO for determining the status of immunization activities, seroprevalence, and disease prevalence, was used. From each province, 30 clusters were selected by using the list of the Provincial Public Registration Office. The number of subjects to be included per group was 25, i.e., the number of subjects in each province (750) divided by the number of clusters (30). The age and sex distribution of these 25 subjects was made to represent the distribution of the general population by using the method of layered sampling with reference to the age and sex distribution of the general population. Thus we aimed to administer 3,000 questionnaires in face-to-face interviews and to collect blood samples for each subject for hepatitis B marker analysis. However, due to the hemolysis of some blood samples, 112 subjects were excluded from the study. Thus the results were derived from a total subject group of 2,888 individuals (96.3% of the original group).

Study design: Before starting the study, approval from the local ethical committee was received, and those subjects over the age of 15 who had consented to participate in the study were included. Informed consent forms as well as information about the aims of the study were provided for each subject.

Age, residence site (rural/urban), level of education, and marital status of the subjects, and any family history of jaundice were recorded.

Blood samples and serologic tests: Blood samples were collected in jelly vacuum tubes under aseptic conditions. These tubes were numbered and sent to the Central Laboratory of the Research Hospital of Dicle University on the day of collection. Sera were centrifuged and stored at −70°C before use. Hepatitis markers were examined by macro enzyme assay (Macro EIA) using an Elecsy 2010 device and kits (Roche, Indianapolis, Ind., USA). HBsAg and Anti-HBs were measured. Blood samples showing positivity for anti-HBs were checked for anti-HBcIgG. Levels of anti-HBs higher than 10 COI (cut-off index), HBsAg higher than 1 COI and AntiHBcIgG lower than 1 COI were accepted as positive.

Definitions: Seropositivity: Exposed to HBV previously; positive HBsAg and/or positive anti-HBs cases with a positive anti-HBcIgG result.

Seronegativity: Unexposed to HBV; cases negative for HBsAg or negative for anti-HBs, or cases with a vaccine history that showed positivity for anti-HBs but negativity for anti-HBcIgG. HBsAg positivity: All cases with a positive HBsAg result. HBsAg negativity: All cases with a negative HBsAg result.

Rural origin: Subjects living in sites with a population below 2,500.

Statistical assessments: Frequency tables were used to evaluate the effects of risk factors on dependent variables of "HBsAg positivity" and "seropositivity". Crude odds ratios and 95% confidence intervals (95% CI) were calculated by chi square testing. Multiple logistic regression analyses were used to calculate adjusted odds ratios and 95% CI. We used EpiInfo to analyze the data.

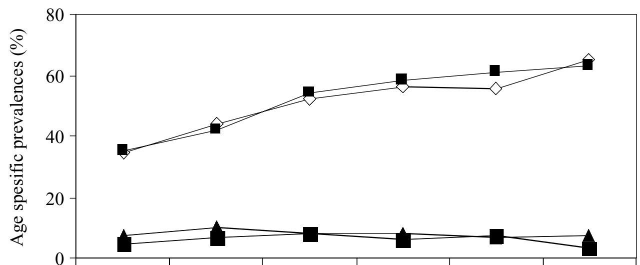
RESULTS

The overall prevalence of HBsAg and the seropositivity in the region were 7.0 and 47.4%, respectively. Thirty-seven percent of the subjects (1,071 individuals) were from rural and 63% (1,817 individuals) were from urban areas. The positive HBsAg prevalence was 8.2% and the seropositivity prevalence was 47.2% in rural areas, and these ratios were 6.2 and 47.4% in urban areas, respectively. There was a significant difference in HBsAg positivity between urban and rural areas (Table 1).

The seropositivity rates increased with age, and there were no differences in the age-specific rates between the rural and urban areas (Fig. 1). The highest prevalence of the previous HBV exposure was in the age group of >64 years both in the rural and urban areas. However, HBsAg positivity did not show the same increase with age. In rural areas, the highest

Table 1. Seropositive and HBsAg positive ratios in urban and rural areas of the southeastern region of Turkey, 2003

	Rural (%)	Urban (%)	*P* odds ratio (95%CI)	Total (%)
HBsAg (–)	983 (91.8)	1,704 (93.8)	0.04	2,687 (93.0)
HBsAg (+)	88 (8.2)	113 (6.2)	0.74 (0.55 - 0.98)	201 (7.0)
Seronegative	565 (52.8)	955 (52.6)	0.91	1,520 (52.6)
Seropositive	506 (47.2)	862 (47.4)	1.00 (0.86 - 1.17)	1,368 (47.4)
Total	1,071 (37.1)	1,817 (62.9)		2,888



	15-24	25-34	35-44	45-54	55-64	>64
Seropositivity in Rural	34.9	44.4	52.4	56.4	55.8	65
Seropositivity in Urban	35.3	41.8	54.5	58.1	60.7	63
HBsAg Positivity in Rural	7.2	10.5	7.8	7.9	6.5	7.5
HBsAg Positivity in Urban	4.9	6.5	8.3	6.2	7.4	3.4

Age groups

Fig. 1. Age specific prevalences of seropositivity and HBsAg positivity in rural and urban areas of the southeastern region of Turkey, 2003.

prevalence of HBsAg positivity was 10.5% in the age group of 25 - 34 years. In urban areas, however, the highest level of HBsAg seropositivity was 8.3% in the age group of 35 - 44 years. There was a significant differences in the prevalence of HBsAg between urban and rural areas, and this difference was clearest in the age groups of 25 - 34 and >64 years.

In Table 2, risk factors for exposure to HBV in urban and rural areas are shown separately. Both in rural and urban areas, male sex was found to be an important risk factor for HBV exposure. In rural areas, 51.4% of the males were infected, and the risk was 1.64 (95% CI: 1.15 - 2.33) times higher than in females. In the urban areas, 49.2% of the males were infected, and the risk was 1.40 higher than in females (95% CI: 1.06 - 1.84). Another risk factor associated with

Table 2. Some of risk factors for HBV infection in rural and urban areas of the southeastern region of Turkey, 2003

	Rural areas			Urban areas		
	n_1 (%)	crude odds ratio (95%CIs)[1)]	adjusted odds ratio (95% CIs)[2)]	n_2 (%)	crude odds ratio	adjusted odds ratio (95% CIs)[2)]
Sex						
female	237 (43.2)	1	1	422 (45.8)	1	1
male	269 (51.4)	1.39 (1.09 - 1.76)[3)]	1.64 (1.15 - 2.33)[3)]	440 (49.2)	1.14 (0.95 - 1.37)	1.40 (1.06 - 1.84)[3)]
Age groups						
15 - 24	106 (34.9)	1	1	171 (35.3)	1	1
25 - 34	118 (44.4)	1.49 (1.05 - 2.12)[3)]	1.47 (1.02 - 2.10)[3)]	206 (41.8)	1.32 (1.01 - 1.72)[3)]	1.24 (0.94 - 1.62)[3)]
35 - 44	94 (52.5)	2.07 (1.39 - 3.06)[3)]	2.09 (1.37 - 3.18)[3)]	177 (54.5)	2.20 (1.63 - 2.96)[3)]	1.90 (1.39 - 2.59)[3)]
45 - 54	93 (56.4)	2.41 (1.61 - 3.62)[3)]	2.41 (1.53 - 3.80)[3)]	151 (58.1)	2.54 (1.85 - 3.51)[3)]	2.07 (1.47 - 2.91)[3)]
55 - 64	43 (55.8)	2.36 (1.38 - 4.05)[3)]	2.29 (1.29 - 4.07)[3)]	82 (60.7)	2.84 (1.88 - 4.29)[3)]	2.16 (1.41 - 3.31)[3)]
>64	52 (65.0)	3.47 (2.01 - 6.01)[3)]	3.17 (1.75 - 5.72)[3)]	75 (63.0)	3.13 (2.02 - 4.85)[3)]	2.21 (1.39 - 3.51)[3)]
Education level						
illiterate	223 (51.1)	1.44 (0.99 - 2.09)	1.03 (0.70 - 1.50)	355 (56.1)	1.91 (1.50 - 2.42)[3)]	1.66 (1.26 - 2.19)[3)]
primary school	213 (45.4)	1.14 (0.79 - 1.66)	1.24 (0.79 - 1.94)	287 (45.2)	1.23 (0.97 - 1.57)	1.23 (0.97 - 1.56)
high school or more	70 (42.2)	1	1	220 (40.1)	1	1
Familial jaundice history						
yes	103 (52.8)	1.31 (0.96 - 1.79)	1.41 (1.02 - 1.95)[3)]	209 (52.3)	1.28 (1.02 - 1.59)[3)]	1.35 (1.07 - 1.70)[3)]
no	403 (46.0)	1	1	653 (46.1)	1	1

[1)]: Crude odds ratios and 95% CIs were calculated by using chi square analyse.
[2)]: Adjusted odds ratios and 95% CIs were calculated by using logistic regression analyze.
[3)]: $P < 0.05$.
n_1: Those were exposed to HBV infection (seropositive subjects) in rural areas.
n_2: Those were exposed to HBV infection (seropositive subjects) in urban areas.

Table 3. Risk factors for HBsAg positivity in rural and urban areas of the southeastern region of Turkey, 2003

	Rural areas			Urban areas		
	n_1 (%)	crude odds ratio (95%CIs)[1)]	adjusted odds ratio (95% CIs)[2)]	n_2 (%)	crude odds ratio	adjusted odds ratio (95% CIs)[2)]
Sex						
female	37 (6.8)	1	1	49 (5.3)	1	1
male	37 (9.8)	1.49 (0.96 - 2.32)	1.83 (1.07 - 3.14)[3)]	64 (7.2)	1.37 (0.94 - 2.01)	1.55 (1.01 - 2.38)[3)]
Age groups						
15 - 24	22 (7.2)	1	1	24 (4.9)	1	1
25 - 34	28 (10.5)	1.51 (0.81 - 2.61)	1.27 (0.43 - 3.72)	32 (6.5)	1.33 (0.75 - 2.38)	1.80 (0.58 - 5.53)
35 - 44	14 (7.8)	1.09 (0.51 - 2.29)	1.57 (0.58 - 4.25)	27 (8.3)	1.74 (0.95 - 3.19)	2.31 (0.77 - 6.91)
45 - 54	13 (7.9)	1.10 (0.51 - 2.35)	1.15 (0.40 - 3.15)	16 (6.2)	1.26 (0.63 - 2.52)	2.86 (0.96 - 8.54)
55 - 64	5 (6.5)	0.89 (0.28 - 2.60)	1.09 (0.38 - 3.08)	10 (7.4)	1.54 (0.67 - 3.47)	2.09 (0.68 - 6.46)
>64	6 (7.5)	1.04 (0.36 - 2.83)	0.87 (0.25 - 3.04)	4 (3.4)	0.67 (0.19 - 2.08)	2.35 (0.71 - 7.74)
Education level						
illiterate	34 (7.8)	0.85 (0.43 - 1.69)	0.77 (0.36 - 1.69)	41 (6.5)	1.12 (0.68 - 1.85)	1.40 (0.81 - 2.42)
primary school	39 (8.3)	0.91 (0.47 - 1.79)	0.79 (0.43 - 1.42)	40 (6.3)	1.09 (0.66 - 1.80)	1.10 (0.68 - 1.78)
high school or more	15 (9.0)	1	1	32 (5.8)	1	1
Familial jaundice history						
yes	26 (13.3)	2.02 (1.24 - 3.28)[3)]	2.15 (1.30 - 3.56)[3)]	32 (8.0)	1.43 (0.94 - 2.19)	1.48 (0.96 - 2.27)
no	62 (7.1)	1	1	81 (5.7)	1	1

[1)]: Crude odds ratios and 95% CIs were calculated by using chi square analyse.
[2)]: Adjusted odds ratios and 95% CIs were calculated by using logistic regression analyze.
[3)]: $P < 0.05$.
n_1: Those were exposed to HBV infection (seropositive subjects) in rural areas.
n_2: Those were exposed to HBV infection (seropositive subjects) in urban areas.

seropositivity was age. Both in urban and in rural areas, the risk ratios increased with age. The highest seropositivity rates were in the age groups of >64 years, both in rural (65%) and in urban areas (63%). Education level had a statistically significant effect on seropositivity in the urban areas but not in the rural areas. In the illiterate group, the seropositivity prevalence was 56.1% and the adjusted odds ratio was 1.66 (95% CI: 1.26 - 2.19). In the rural areas, 51.1% of the illiterate people were found to be seropositive. This ratio was higher than that in the educated groups, but the difference was not statistically meaningful. The seropositivity rates were higher in the group with a positive familial jaundice history than in the group without a familial jaundice history, in both the rural and urban areas.

Table 3 shows the risk factors for HBsAg positivity. In the rural areas, 9.8% of the men and 6.8% of the women were positive for HBsAg, and in the urban areas these ratios were 7.2 and 5.3%, respectively. Male sex was thus determined to be an important risk factor for HBsAg positivity. HBsAg positivity did not differ among age groups. There was no difference in HBsAg positivity between the different education-level groups. In urban and rural, there was discordance in HBsAg positivity in terms of education level. Although the highest prevalence of HBsAg positivity was in the higher educated group (9.0%) in the rural areas, the highest prevalence was in the illiterate group in the urban areas. Familial jaundice history was an important risk factor in the rural areas. The prevalence of HBsAg positivity was 13.3% in the group with a positive familial jaundice history. Although there was no statistically significant difference between the groups with and those without a family history of jaundice in the urban areas, in the group with familial jaundice the prevalence of HBsAg positivity (8.0%) was higher than that in the group without a family history of jaundice (5.7%).

DISCUSSION

This study showed that the prevalence of HBV infection in the southeastern region of Turkey is at an intermediate level. The ratio of HBsAg positivity, which might represent chronically HBV carriers, was 7% for this southeastern region, and this ratio was higher in rural than in urban areas (8.2% versus 6.2%). In general, the route of viral infection in developing countries is not clear. We tried to identify the routes and risk factors for HBV infection in the present study. Although hepatitis virus infection is now a major problem in developing countries, no detailed epidemiological information has been obtained for this virus in Turkey. Overall exposure to hepatitis is also an important indicator of epidemiologic pattern of the disease. In this study, all cases that tested positive for HBsAg and positive for anti-HBs, with the exception of those that tested negative for anti-HBcIgG, were regarded as having been exposed to HBV. Exposure rate for HBV also was not low in the southeastern region of Turkey. The comparison of the prevalence rates and risk factors of rural with urban areas may suggest public health workers to develop specific strategies according to different regions. Although the rate of HBsAg positivity differed between the urban and rural areas, that of HBV exposure did not. This result may have been due to the fact that maternal transmission is more prevalent in rural areas. One of the distinctive features of HBV infection is that the risk of chronicity varies greatly with the age at which the infection is acquired. For neonates and children younger than 12 months of age who acquire the infection, the risk of the infection becoming chronic is 90% (10), and in those parts of the world with an intermediate endemicity of HBV infection, transmission in infancy, early childhood, and adulthood maintains the level of chronic infection (11).

Male sex was an important risk factor for both HBsAg positivity and exposure rate. These results show that there have been major transmission routes of HBV infection other than the vertical route in both rural and urban areas. In resource-poor countries, where most HBV infection occurs early in life, sexual transmission is still relevant for adults (12). In developing countries, particularly in Islamic regions, multi partnership is unusual in women. In Turkey, risk factors such as multi partnership, intravenous drug usage, having shave in common barbers, traveling, etc. are more prevalent in men than in women, which may explain the higher rate of HBsAg positivity or higher rate of HBV exposure in men. In many other reports in Turkey, the HBsAg positivity rate was higher in men (13-15).

Although illiteracy was not a significant factor in HBV infection in rural areas, HBV seropositivity was higher in illiterate persons in urban areas. In multivariate analyses, viral infections were independently associated not only with behaviors such as IV drug usage and commercial sex but also with low income and education levels (16). In urban areas, preventive measures are more available than in rural areas, but the use of these health facilities increases with the education level. People with a higher level of education tend to use health services like health education, vaccination, and high quality dentistry services, etc. A previous study reported that the prevalence of hepatitis C, which has the same transmission route as hepatitis B, was greater for donors who had an educational level of 8th grade or less, and it was noticed that socioeconomic status and its association with increased susceptibility to infectious agents could account for a portion of the increased HCV seroprevalence seen in poorly educated, black or Hispanic middle-aged blood donors (17).

In the region of Amazon out of 258 contacts of 97 index cases with HBV infection, 51.6% had serological markers of past infection; the authors stated the importance of intrafamilial transmission of HBV infection (18). There are many other reports showing evidence of familial transmission of HBV and chronically complicated of HBV infection (19-21). Evidence showing familial transmission of HBV was significant effect of familial jaundice on to the HBV positivity and HBsAg positivity. A positive family history of jaundice resulted in a twofold increase in rural areas. Risk factor of positive familial jaundice had an important effect in rural area. In rural families are more crowded this may be increasing familial transmission. But also we need other detailed studies to explain why familial transmission is more prevalent in rural.

We could not determine the dominant genotype of HBV in the region because we did not have enough technical equipment. This was the one of the limitations of our study. But in a recent study it was reported that genotype D was dominant in the region (22).

The results indicate that the southeastern region of Turkey may be considered an area of intermediate endemicity for HBV infection. There was no substantial difference in prevalence of HBV infection exposure between the rural and urban populations. The HBsAg positivity was higher in rural areas than urban areas. Although education level was an important risk factor in urban areas it was not in rural areas. Both in urban and rural areas, male sex, higher age, and positive family history of jaundice may be considered to important risk factors.

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