# Heterogeneous distribution of hepatitis B serological markers in rural areas of Mexico

Luis A Juárez-Figueroa, MD,[1] Felipe Javier Uribe-Salas, MD,DSc,[2] Carlos Jesús Conde-González, M Sc, PhD.[3]

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## Abstract

**Objective**. To study the distribution of the hepatitis B antibody (anti-HBc) based on a national serosurvey from 10 Mexican states showing a mean HBV prevalence higher than the national one. **Materials and Methods**. This was a cross-sectional study. During 2003, anti-HBc was analyzed at INSP in 19 907 sera, and the related sociodemographic factors were determined. **Results**. Anti-HBc prevalence was greater among men, but it was also associated to age, residence in a rural area, low socio-economic status, and illiteracy. Clusters of very high anti-HBc prevalence were found in several rural communities where the prevalence of anti-HBc in adults is 3 to 20 times the national average. **Conclusions**. Besides a low endemicity of HBV in Mexico, distribution is heterogeneous as was shown in several of the states studied, where there are rural towns with very high prevalence of HBV markers. National serosurveys are useful tools for identifying communities with hepatitis B hyperendemicity, where focused research and control measures are needed.

Key words: Hepatitis B; rural Mexico; anti-HBc; Mexico

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## Resumen

**Objetivo**. Estudiar la distribución de anti-HBc en 10 estados con prevalencia mayor a la media nacional en la ENSA 2000. **Material y métodos**. Durante 2003 se analizó en el INSP anti-HBc en 19 907 muestras de suero, se determinaron factores sociodemográficos relacionados. **Resultados**. La prevalencia de anti-HBc fue mayor en hombres. Se asoció con la edad, residencia en áreas rurales, bajo nivel socioeconómico y analfabetismo. Se encontraron agrupamientos de alta prevalencia de anti-HBc en comunidades rurales en las cuales la prevalencia de anti-HBc en adultos está entre 3 y 20 veces por arriba de la media nacional. **Conclusiones**. Contrastando con la baja endemicidad del VHB en México, su distribución es heterogénea. En varios estados se hallaron localidades rurales con muy alta prevalencia de anti-HBc. Las encuestas de salud permiten identificar comunidades donde la hepatitis B es hiperendémica y en las cuales se requiere enfocar la investigación y tomar medidas de control.

Palabras clave: hepatitis B; México rural; anti-HBc; México

(1) Programa de VIH/SIDA de la Ciudad de México.
(2) El Colegio de la Frontera Norte, México.
(3) Instituto Nacional de Salud Pública, México.

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Address reprint requests to: Dr. Luis Juárez-Figueroa. Laboratorio de VIH/ETS, Programa de VIH/SIDA, Ciudad de México. Benjamín Hill 24, Col. Condesa, 06140 México DF.
E-mail: luisjuarez@insp.mx

The infection caused by the hepatitis B virus (HBV) has a different epidemiologic, demographic and geographic distribution in human populations. Some authors have documented[1,2] that in the Americas, Mexico is still a low endemic country regarding the HBV infection, and the prevalence of HBV carriers in our country has been low. The first Mexican national serological survey conducted in 1974 used the HbsAg marker, and it estimated that 0.3% of the general population corresponded to HBV carriers.[3] Even among persons with high-risk sexual behavior, such as commercial sex workers, the prevalence of the *s* viral antigen has been low, ranging from 0.2% in 1988 to 0.8% in 1998.[4-7] Women seeking HIV antibodies testing during 1992 in Mexico City showed an HBsAg prevalence of 0.2%.[8] Among college students from the state of Nuevo Leon, the global HBsAg seroprevalence was 0.39% in 1996.[9]

HBV carriers in Mexico can be found among men who have sex with men and, to a lesser extent, among care workers. One study carried out in Mexico City reported the following HBsAg prevalences according to the sexual practices of men: among men who have sex only with females, 0.3%; among those who have sex with females and males 1.1%; and among those who have sex only with males, 4.8%.[10] Furthermore, one multicentric survey among 935 care workers in Mexico reported a global HBsAg prevalence of 1.2% with variations in terms of occupation: nurses, 0.6%; odontologists, 1.5%; physicians, 2%; and laboratory technicians, 2.5%.[11]

HBV transmission by blood transfusion decreased when the Mexican government banned the commercialization of blood and established blood screening using HBsAg detection. Once this practice became compulsory in 1986, this form of HBV transmission was virtually eliminated.[12,13] Further studies among blood donors in Mexico have reported HBsAg prevalences ranging from 0.13% to 0.34%.[14-16]

Some years ago in Mexico, anti-HBc and HBsAg markers from the 2000 National Health Survey (ENSA 2000), a nationwide population-based survey, were analyzed. Overall HBV seroprevalence with both markers was 3.3% and 0.21%, respectively.[17] In this regard, a question that has not been answered yet is whether the distribution of the HBV infection is homogeneous in Mexico. The present study analyzes characteristics associated with the HBV infection in the 10 states whose anti-HBc prevalence among adults is greater than 5%, i.e., 1.7 percent points higher than the national average. Anti-HBc is a marker that identifies individuals with previous or current HBV infection, and it constitutes an epidemiological tool to estimate the prevalence of exposure to HBV infection in the population. We hypothesize that the HBV infection in the Mexican population is not homogenous, and that one indicator of this assertion is that variations in HBV seroprevalence as assessed by anti-HBc testing depend on urban versus rural residence.

## Materials and Methods

### Study design and selection of the population

The ENSA 2000 studied a multistage stratified cluster sample of non-institutionalized civilian population of Mexico including children (0-9 years of age), adolescents (10-19 years of age) and adults (≥ 20 years of age). The final sample size of the survey was useful to make estimations both at national and state level regarding the 32 federal entities or states that constitute the country.[18] The 90 916 persons selected from the sample frame (26.6% children, 23.5% adolescents and 49.8% adults) were interviewed at their home and a blood sample was taken from each after an informed consent had been signed.

There were 83 157 serum samples available (91.4%) from all the individuals interviewed.[18] For this study we selected all the subjects from the adolescent and adult populations of those states whose anti-HBc prevalence among adults was higher than 5% with respect to the sample frame of the ENSA 2000. The distribution of population by state and the prevalence of the Anti-HBc marker by state and by age group are shown in Table I. The final number of samples analyzed in this study (n = 19 898) represented almost one third of the total samples collected by the ENSA 2000.

### Questionnaire, variables and ethical considerations

The ENSA 2000 obtained information on the following issues: socio-demographic characteristics of the population; risk factors for chronic diseases; biological markers of infectious diseases; and access, use and coverage of health service programs.[18] For this work, the following socio-demographic characteristics of the adult population were studied: age, sex, place of residence, literacy, and goods index. The protocol for this study was approved by the Ethics Committee at the National Institute of Public Health (INSP) in Mexico, and the data were gathered under the confidential principles stated by the Statistical and Geographical Information Law.[19]

### Estimation of seroprevlaence of HBV and laboratory analyses

Anti-HBc was used as a marker of previous and/or current HBV infection among 6 378 adolescents

**Table I**
**Anti-HBc prevalence in 10 Mexican states from ENSA 2000. 2003**

| State | Adolescents (10-19 years) | | | Adults (20 years or more) | | |
|---|---|---|---|---|---|---|
| | N | *Prev % | (CI 95%) | N | *Prev % | (CI 95%) |
| Campeche | 647 | 1.1 | (0.4-2.2) | 1377 | 7.0 | (5.7-8.5) |
| Colima | 615 | 0.3 | (0.2-1.2) | 1348 | 8.8 | (7.4-10.5) |
| Chiapas | 586 | 0.9 | (0.4-2.0) | 1321 | 9.0 | (7.5-10.7) |
| Guerrero | 652 | 2.5 | (1.4-3.9) | 1343 | 11.2 | (9.5-13.0) |
| Morelos | 599 | 0.2 | (0.0-0.9) | 1380 | 5.1 | (4.0-6.4) |
| Nayarit | 694 | 0.3 | (0.1-1.0) | 1420 | 8.9 | (7.4-10.5) |
| Oaxaca | 629 | 0.2 | (0.0-0.8) | 1308 | 5.6 | (4.4-7.0) |
| Sinaloa | 668 | 0.4 | (0.1-1.3) | 1348 | 9.5 | (8.0-11.2) |
| Tabasco | 661 | 0.8 | (0.2-1.7) | 1367 | 5.8 | (4.6-7.1) |
| Yucatán | 627 | 0.5 | (0.1-1.4) | 1308 | 9.4 | (7.9-11.1) |

*Prevalence percent (Confidence interval 95%)
ENSA 2000: National Health Survey 2000

(10-19 years of age) and 13 520 adults (≥ 20 years of age). Preliminary sample screening for anti-HBc was conducted at INSP using pooled samples (aliquots of equal volume) of three sera. Anti-HIV was also assessed in the same pooled samples. Single sera of all positive pooled samples were afterwards analyzed to determine individual seropositivity.

### Statistical analyses

A descriptive analysis was performed to estimate the prevalence of anti-HBc by stratifying the variables by sex and by state. To estimate the magnitude of the association between anti-HBc prevalence and the study variables, we calculated prevalence odds ratios and their corresponding confidence intervals. We conducted crude and multivariate analyses using a logistic regression model that included all the study variables. These data analyses were performed using the STATA 9.0 software.* A map was drawn using the geographical information system Arc View 9.0 to project the geographic distribution of anti-HBc antibody among adults at a municipal level (Figure 2).

* Stata Survey Data, 2003. Reference Manual. Release 8, Stata Corporation, United States of America

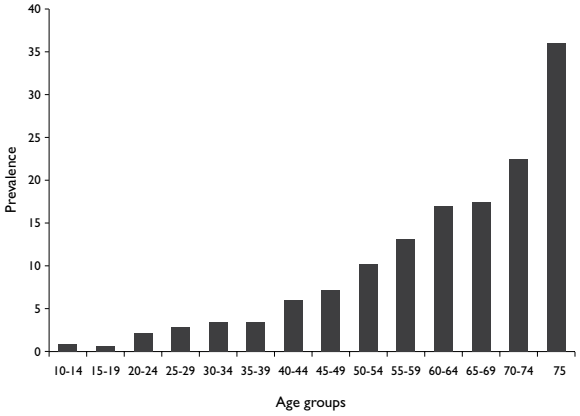


**Figure 1.- Anti-HBc prevalence by age from 10 States (ENSA 2000). 2003**

## Results

We studied 19 898 individuals out of which 13 520 (68%) were adults. The global prevalence of anti-HBc among young people aged 10 to 19 in the ten states studied was 0.7%, while among individuals aged 20 or more it was 8.0%. The prevalence of anti-HBc among adolescents and adults stratified by state is shown in Table I. Prevalence increased with age, from less than 1% in the 10 to 14

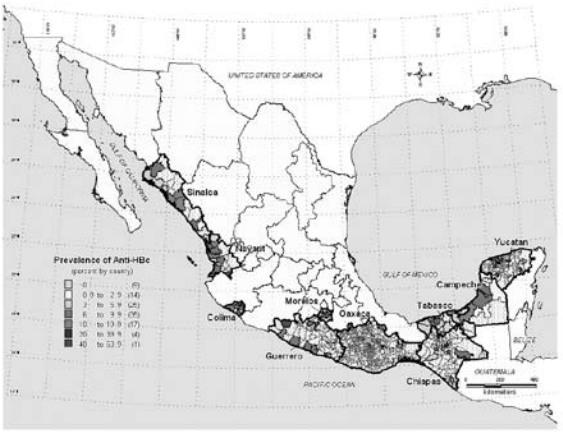


**Figure 2. Prevalence of Anti-HBc**

years-of-age group to 36% in the group > 75 years of age (Figure 1). Only two of the anti-HBc positive individuals (from a total of 1 130) were also found to be anti-HIV positive (0.18%).

Prevalence of anti-HBc among adults was significantly greater in men than in women. Anti-HBc positivity was also associated with age, residence in a rural area, low socio-economic status and lack of education ($p < 0.001$) (Table II).

When distribution of prevalence of the anti-HBc marker was analyzed with respect to the rural communities in the selected states, the results show that in twelve communities belonging to seven of the studied states prevalence among adults was higher than 31% (Table III). Three communities from the state of Guerrero displayed the highest prevalences, ranging from 72% to 90%. Other states displayed lower prevalences than Guerrero, but they were nevertheless much higher than the average reported among the adult population by the ENSA 2000 (3.3%).[17] The third column in Table III represents the total population of communities according to the 12th National Census of Population and Housing performed in 2000. The number of inhabitants points to their rural character. Prevalences were estimated by using information from the ENSA 2000 sample frame (data no shown). Figure 2 represents a quite heterogeneous distribution of anti-HBc prevalences within each state studied.

## Discussion

Results from the ENSA 2000 samples indicate that the highest HBV prevalence is observed along the Pacific coast, the southern border region, and in the states south of the Gulf of Mexico. This distribution pattern was first observed in 1974 following Mexico's first national seroepidemiological survey.[3] Data presented herein indicate that distribution of HBV in Mexico is heterogeneous with apparent rural clusters. Very low and very high prevalence counties may be found within the same state (Figure 2).

Anti-HBc prevalence increases significantly from adolescence onwards, which suggests that HBV transmission in Mexico most likely concurs with the onset of sexual relations. Among adults, HBV affects men more than women, which points to the existence of a differential risk, associated with sexual-related behaviors not studied by the ENSA 2000. Anti-HBc prevalence is higher in rural areas than in urban ones, and it is associated with age, lack of schooling and low socio-economic status.

In the 10 states (from ENSA 2000), only two out of the 1 130 individuals found to be anti-HBc positive also tested positive for anti-HIV antibodies (0.18%), suggesting that the behavior of the AIDS epidemic in this group is not different from the one observed in the population at large.[20] Other population groups in Mexico, however, such as urban men who have sex with men, show high prevalence for both HBV and HIV.[10] In such groups, the presence of one of these infections predicts the other, since they are both associated to the same risky sexual behavior as has been demonstrated in cohort studies.[21,22]

Rural communities where anti-HBc prevalences were 3 to 20 times higher than the national average were identified based on the ENSA 2000. A very high prevalence of HBV serological markers was further confirmed in two of these rural villages, Calera and Cuambio (Table III,) where an average anti-HBc prevalence of 50.5% was found in a larger sample from the population > 11 years of age.[23]

Given the large proportion of clustered individuals testing positive for anti-HBc antibodies, an alternative hypothesis regarding the iatrogenic transmission of the virus mainly in rural areas could point to the reuse of syringes and needles. The World Health Organization has warned that on a daily basis, unsafe injections cause a steady number of unrecognized transmissions of blood-borne infections in developing countries, and that the distribution of such injections appears to be strongly clustered within the population of each country,[24] which is consistent with the HBV distribution pattern found in this study. Carrying on with the study of these and other communities, using tools such as ethnographic descriptions, in-depth interviews and identification of key informants from each community in order to better understand the role of unsafe injections, risky sexual behavior, migration and other factors in the spread of

**Table II**
**Characteristics asociated with anti-HBc antibody in adults from 10 Mexican states with high prevalence from ENSA 2000, 2003**

| *Characteristic* | *N* | **Prev. %* | *‡OR (CI 95%)* | *§OR (CI 95%)* |
|---|---|---|---|---|
| *Sex* | | | | |
| Women | 9304 | 7.0 | 1.0 | |
| Men | 4216 | 10.2 | 1.5 (1.3-1.7) | 1.3 (1.1-1.4) |
| *Age in years* | | | | |
| 20-29 | 3720 | 2.1 | 1.0 | |
| 30-39 | 3273 | 3.4 | 1.6 (1.2-2.2) | 1.6 (1.2-2.2) |
| 40-49 | 2507 | 6.7 | 3.3 (2.5-4.3) | 3.3 (2.5-4.4) |
| 50-59 | 1761 | 11.5 | 6.0 (4.6-7.8) | 5.9 (4.5-7.8) |
| 60-69 | 1234 | 17.3 | 9.7 (7.4-12.6) | 9.4 (7.1-12.3) |
| 70 or more | 1025 | 30.2 | 20.0 (15.4-25.9) | 18.6 (14.2-24.3) |
| *Place of residence* | | | | |
| Urban | 5735 | 7.0 | 1.0 | |
| Rural | 7785 | 8.8 | 1.3 (1.1-1.5) | 1.2 (1.0-1.4) |
| *Reading knowledge* | | | | |
| Yes | 11288 | 6.7 | 1.0 | |
| No | 2223 | 14.7 | 2.4 (2.1-2.7) | 1.2 (1.0-1.4) |
| *Goods possession index* | | | | |
| High | 2677 | 5.9 | 1.0 | |
| Middle | 6847 | 7.7 | 1.3 (1.1-1.6) | 1.3 (1.1-1.6) |
| Low | 3946 | 9.9 | 1.8 (1.5-2.1) | 1.6 (1.3-2.0) |

* Prevalence %
‡ Crude odds ratio
§ Odds ratio adjusted with all variables
ENSA 2000: National Health Survey 2000

the VHB infection might prove to be appropriate. Since universal hepatitis B vaccination of newborns started in Mexico in 1999, vaccination against hepatitis B for those aged over 10 in these high-prevalence communities is expected to be minimal, and it points to the urgent need to offer such vaccination to adolescents and young adults in the communities studied.

In conclusion, national health surveys are an ideal tool to identify populations at risk of hepatitis B. Unlike urban population groups with high concurrent prevalence of HBV and HIV, such as men who have sex with men,[10] the hepatitis B epidemic in rural areas has largely developed to date without the presence of HIV. The older age groups are the most seriously affected, pointing to the historical nature of the epidemic, which is probably in decline. However, the existence of relatively isolated rural towns where conditions currently exist for HBV transmission, as demonstrated by the presence of anti-HBc positivity among young people, reinforces the need for a continued surveillance and for the implementation of preventive interventions in such localities.

*Declaration of conflicts of interest:* The authors declare no conflict of interest.

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**Table III**
**Rural communities with high anti-HBc antibody prevalence among adults from ENSA 2000**

| *State* | *Community* | **Population* | *Anti-HBc prevalence (%)* |
|---|---|---|---|
| Campeche | Quetzal Edzná | 327 | 60 |
| Chiapas | Tzeltal | 1275 | 33 |
| | San Nicolás Buena Vista | 290 | 43 |
| Colima | Jala | 569 | 43 |
| Guerrero | La Calera | 470 | 76 |
| | Cuambio | 226 | 72 |
| | El Terrero | ‡ | 90 |
| Sinaloa | El Alamito | 163 | 45 |
| Tabasco | Dos Ceibas | 1171 | 62 |
| Yucatán | Nolo | 1369 | 36 |
| | Ekmul | 1901 | 54 |
| | Jubila | 255 | 31 |

* Number of inhabitants, national census year 2000
‡ Not covered by the national census
ENSA 2000: National Health Survey 2000

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