Epidemiology of hepatitis B in the Islamic Republic of Iran

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وبائيات التهاب الكبد البائي في جمهورية إيران الإسلامية

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خلاصة : إن التهاب الكبد البائي ، الذي هو سبب شائع لالتهاب الكبد الفيروسي ، يستنفذ قدراً كبيراً من موارد البلدان النامية . وقد تم تحليل المعطيات المستقاة من « المسح الصحي والمرضي في جمهورية إيران الإسلامية » فيما يتعلق بوبائيات حَمَلة التهاب الكبد البائي . وكان القصد من هذه الدراسة تقييم انتقاله كمرض تنتقل عدواه في أوساط المجتمع المحلي . وقد أجريت اختبارات للمستضد السطحي لالتهاب الكبد البائي على أمصال 39841 شخصاً ، وتم تحديد تأثير عوامل عديدة على معدل انتشار حملة فيروس التهاب الكبد البائي . وقد تراوحت نسبة حامليه بين صفر و3,9% أي بمتوسط قدره 1,7% . وتبين أن الذكور الأكبر سناً الذين يعيشون في القرى التي تتسم بتدني المستوى الاجتماعي الاقتصادي وسوء الاصحاح وزيادة الاختلاط بين الأسر ، هم أكثر المساهمين في ارتفاع معدل الإصابة بالتهاب الكبد البائي في البلاد .

ABSTRACT Hepatitis B virus, a common cause of viral hepatitis, consumes a large portion of health resources in developing countries. Data obtained from the Survey of Health and Disease in the Islamic Republic of Iran were analysed with respect to hepatitis B-carrier epidemiology. Since the precise mode of transmission of hepatitis B is not well known, the study was designed to evaluate its transmission as a community-acquired disease. HBsAg tests were performed on the sera of 39 841 persons and the impact of several factors on the prevalence rate of HBV carriers was determined. The rate of hepatitis B carriers varied between zero and 3.9% with an average of 1.7%. Older males living in a village with low socioeconomic status, poor sanitation and intrafamily contact are the most important contributors to the rise of hepatitis B infection in the country.

Epidémiologie de l'hépatite B en République islamique d'Iran

RESUME L'infection par le virus de l'hépatite B, cause fréquente de l'hépatite virale, absorbe une grande partie des ressources sanitaires dans les pays en développement. Les données provenant de l'enquête sur la santé et la morbidité en République islamique d'Iran ont été analysées en ce qui concerne l'épidémiologie de l'hépatite B relativement aux porteurs du virus. Le mécanisme exact de transmission de l'hépatite B n'étant pas bien connu, le but de cette étude était d'évaluer la transmission de cette affection en tant que maladie contractée dans la collectivité. Des tests de recherche de l'antigène de surface de l'hépatite B (HBsAg) ont été réalisés sur les sérums de 39 841 personnes, et l'impact de plusieurs facteurs sur le taux de prévalence des porteurs du virus de l'hépatite B a été déterminé. Le taux de porteurs de l'hépatite B variait de zéro à 3,9%, avec une moyenne de 1,7%. Les hommes d'un certain âge vivant dans les villages, ayant un faible niveau socio-économique, des conditions médiocres d'assainissement et des contacts dans le milieu familial sont ceux qui contribuent le plus à la progression de l'hépatite B dans le pays.

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has become a reality. Nevertheless, AIDS cases due to blood transmission will continue to occur in individuals who were infected many years ago but have not yet developed disease.

Mobilizing and sustaining the resources required to ensure blood safety pose a constant challenge to the developing countries. It would be wise to use the available resources judiciously. Priorities in blood safety should include universal screening of blood for HIV antibodies using sensitive tests, promotion of voluntary nonremunerated blood donations, donor deferral and appropriate use of blood. More sophisticated tests such as PCR and antigen tests are expensive and are not recommended until they become affordable.

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Introduction

Hepatitis is the major cause of liver disease and hepatocellular carcinoma. A large number of cases are seen in eastern Asia and sub-Saharan Africa [*1,2*], where two of the most important health problems are chronic liver disease and liver cancer [*2,3*]. Up to 80% of liver cancers are believed to result from this viral infection which is the most important cause of cancer mortality worldwide after smoking. The prevalence of hepatitis B carriers varies in different parts of the world, ranging from less than 1% to 15%. In the Middle East, the endemicity is intermittent, with a carrier rate of 2% to 7% [*1,2,3,4*].

Materials and methods

Data for this study were derived from the results of the Survey of Health and Disease in the Islamic Republic of Iran. A sample containing 1/1000 of the population from all parts of the country was used. Families in clusters of seven neighbouring families were selected randomly in each urban or rural area. Family members aged between 2 years and 69 years were included in the study.

Data were collected over a period of one year (November 1990–November 1991). The collection procedure involved filling questionnaires by a coding method. Each team consisted of two physicians, a dentist, a laboratory technician and a researcher to fill in the questionnaire and collect data from each family. The questionnaire covered sanitary, social and economic status as well as medical history, clinical examination and laboratory test results for each family member.

For hepatitis B surface antigen determination, an *in vitro* diagnostic kit called Hepanostika HBsAg, which is an enzyme immunoassay, was used. The specificity of this method in positive samples was rechecked by Hepanostika-HBsAg confirmatory reagents. Definition of variables has been omitted in this article because of their large number, and only those variables that had a meaningful relation to the state of hepatitis B carriers are described in the results.

Results

After discarding incomplete questionnaires, HBsAg tests were performed on the sera of 39 841 individuals. The total number of positive HBsAg tests was 678 (1.7%). The rate of hepatitis carriers in different provinces of the country varied between zero and 3.9%.

Investigation of individuals on the basis of their area of habitation revealed that the number of carriers in cities was 335 and in rural areas 343, corresponding to 1.5% of urban and 2.0% of rural populations, respectively. The difference observed between urban and rural areas was statistically highly significant ($P < 0.0001$).

Out of 678 positive cases, 324 were females and 354 were males, corresponding to 1.5% of all women and 1.9% of all men, respectively. This difference was also statistically highly significant ($P = 0.0033$).

With respect to age and its role in the prevalence rate of carriers, individuals were divided into several age groups and the prevalence rate in each was calculated (Figure 1). The minimum rate of prevalence (1.2%) was found in the age group 2–9 years; this rate then increased with age and reached its highest level (2.9%) in the age group 50–59 years. The last group showed a relative decrease in the prevalence rate of carriers. Differences among the various age groups were statistically significant.

Another important element was occupation. As shown in Figures 2 and 3, the percentage of carriers among different occupational groups varied, the highest being amongst farmers (3.2%). The classification according to occupation excluded individuals under the age of 20 years.

With regard to level of education, subjects were divided into groups: illiterate, read and write only, elementary education, high school education, and higher education. Figure 4, which shows the carrier prevalence rate within each group regardless of age, illustrates that the carrier rate has an inverse relation with increasing lev-

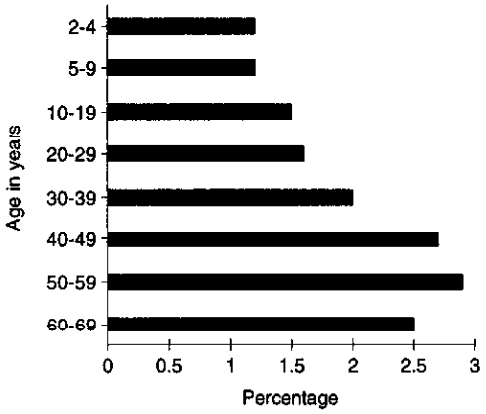

Figure 1 **Prevalence of hepatitis B carriers in different age groups**

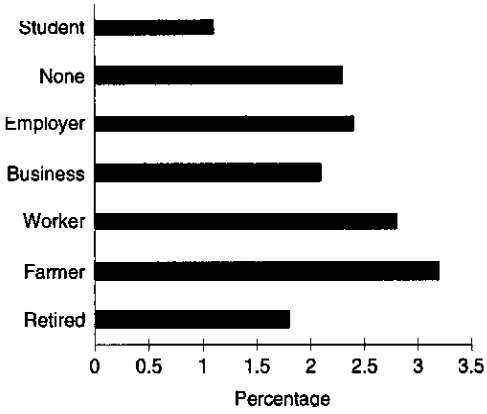

Figure 2 **Prevalence of hepatitis B carriers in men (> 20 years) in different occupations**

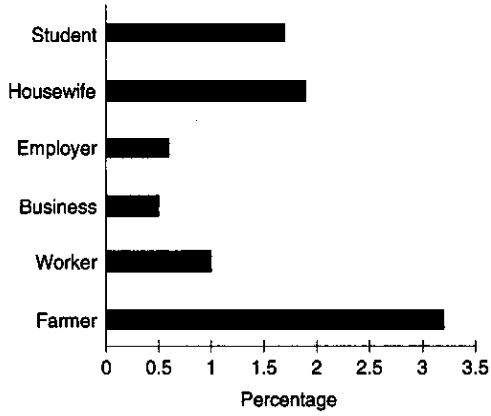

Figure 3 **Prevalence of hepatitis B carriers in women (> 20 years) in different occupations**

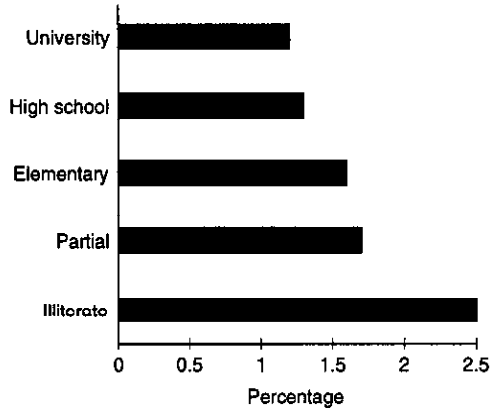

Figure 4 **Prevalence of hepatitis B carriers for different education levels**

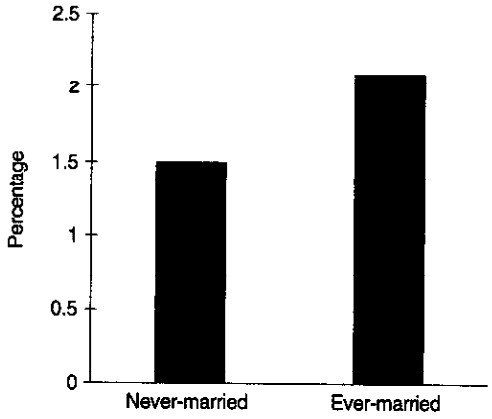

Figure 5 **Prevalence of hepatitis B carriers according to marital status**

el of education. It was interesting to note how age affected these results. To clarify this aspect, subjects were divided into three separate age groups: under 20 years, 20–40 years and above 40 years. In the first group (under 20 years) the level of education rises with age, leading to a larger difference in the prevalence of carriers among various groups. Furthermore, the number of illiterate or partially educated individuals increases with age in the third group (above 40 years of age), and age could be regarded as the only cause of difference. Therefore, to diminish the role of age as a confounding factor, the first and third groups were omitted from the analysis. A statistically significant difference was observed only in the second group (20–40 years) ($P = 0.0032$). The conclusion was that, in addition to age, the level of education was an important factor in determining the prevalence rate of hepatitis carriers, at least in the 20–40 year age group.

With regard to marital status, subjects above 16 years of age were divided into two groups. The first included the ever-married (married, divorced and widowed men and women) and the second consisted of never-married individuals. As is evident from Figure 5, marital status was one of the most important elements determining the prevalence rate of carriers, and the difference was statistically significant ($P = 0.0006$).

To determine the relationship between sanitary and socioeconomic factors and the rate of carrier prevalence, a few elements were chosen as parameters of personal hygiene. These elements were: the use of soap, bathing, tooth-brushing and the type of water consumed. In addition, personal living space calculated by dividing the house area in square metres by the number of family members was used as an indicator of socioeconomic status.

The rate of carrier prevalence among soap users was 1.7% compared with 2.2% among non-users. This difference was statistically significant ($P < 0.01$). Regarding bathing, the prevalence rate of carriers among people who took a shower less than once a week was found to be 2.9% compared with 1.8% among those who showered once or more a week. The difference is statistically significant ($P < 0.0005$). Tooth-brushing was another element that was considered as an indicator of personal hygiene. Prevalence rate of carriers among people who never brushed their teeth or did so only occasionally was 2.1% compared with 1.5% among those who brushed once a day or more, a statistically significant difference ($P < 0.0001$).

When divided into two groups, those using tap water and those who consumed water from fountains, wells, rivers etc., the prevalence rates were 1.7% and 2.2%, respectively. The difference was statistically significant ($P < 0.01$).

To determine the relationship with socioeconomic status, people were divided into three socioeconomic groups: low (< 10 m^2 of living space per person), average (10^2 to 19.99 m^2 per person) and

high > 20 m^2 per person). The carrier prevalence rate was found to be 2.5%, 1.6% and 1.3% in each group, respectively, the difference being statistically significant ($P < 0.0001$). Non-carriers were found to have more living space than carriers, 17.9 m^2 per person as opposed to 15.4 m^2 per person for carriers, the difference being quite significant ($P < 0.0003$). With regard to the importance of socioeconomic status, the question is whether sanitary factors mentioned above influence the carrier prevalence rate independently or are dependent on socioeconomic condition. After eliminating the socioeconomic level, it was revealed that no hygienic factors, such as using soap, brushing teeth and the type of water used, were independent factors in the prevalence rate. Bathing was the only factor that showed a statistically significant correlation with the carrier prevalence rate, even after socioeconomic status was eliminated ($P < 0.01$) as a factor.

Further elaborations on the families of carriers showed that in 30% of the cases more than one member of the family were antigen positive. The relationship among carriers in a given family was as follows: brother and sister (54%), mother and child (29%), father and child (20%), husband and wife (14%). Furthermore, when one of the children in the family was a carrier, there was a 10% risk that other children would be carriers too. When the father or mother was infected, children had a 6% and 8% chance of being carriers, respectively; when both parents were infected, the risk became 21%. In addition, when two children in a family were carriers, the risk of becoming a carrier increased to 28% for the third sibling.

Other factors, such as clinical findings and history of illness, were studied in connection with the prevalence of hepatitis carriers. No relationship was found to exist between the prevalence rate of hepatitis carriers and a positive history of jaundice, urticaria, rash, diabetes or cancer. Other clinical findings, such as hepatomegaly, splenomegaly, abdominal masses, abdominal tenderness, joint disorders and deformities, skin lesions such as psoriasis, eczema, acne, scabies, fungal infection of skin, hair and nails and other abnormalities did not show statistically significant difference in the prevalence rate of hepatitis carriers.

The prevalence rate of hepatitis was 2.0% among those with intestinal parasites and 1.6% for those without this condition, the difference being statistically significant ($P < 0.0078$). However, with respect to each individual pathogenic parasite, no significant differences were observed.

Discussion

In this study significant statistical relationships were observed in the prevalence rate of hepatitis B carrier according to several factors. In all cases, members of the group exhibiting negativity were taken as controls. According to the results of this study, the prevalence rate of HBV carriers in Islamic Republic of Iran is 1.7%. This figure is lower than that of a previous report based on sampling from adult blood donors, although the prevalence rate in the adult age group of this study is approximately the same as in that report. Asia, with a rate of 8%, is a high prevalence region, and with respect to its population of 2.8 billion, is the home for 75% of all carriers. The minimum rate of prevalence in Asia is reported from Kuwait at 1.5%. Other Asian countries fall either in the regions of intermediate prevalence (India, Middle East, west Asia) or in the regions of high prevalence (south-east Asia, China, Korea and the Philippines). The importance of determining the prevalence rate of carriers becomes

evident when determining the modes of transmission and preventive strategies.

In all epidemiological studies. age has proved the most important factor. The age of acquiring infection is the major determinant of the incidence and prevalence rates of HBV. In this study, patients were classified into several age groups with respect to the prevalence of carriers. The difference in various age groups indicates that this factor plays an important role in the prevalence rate.

According to the statistics obtained in this study, the carrier prevalence rates among men and women were 1.9% and 1.5%, respectively. This result is similar to that reported from the Middle East [*5*], Somalia [*6*], Gambia [*7*], Nepal (men 1.5%, women 0.5%) [*8*], South Africa (men 6.1%, women 4.4%) [*9*] and Labrador (men 1.6%, women 1%) [*10*]. In Hong Kong, the prevalence of all types of hepatitis is higher among men than women [*2*]. In a study performed in the United States, the ratio of carrier males to carrier females in childhood was reported to be 1:1.4; this ratio is 2:1 in adulthood [*1*]. The reason for the observed difference is not yet clear. Some believe it is due to a higher probability of the infection becoming chronic in men compared to women, rather than the higher rate of infection among men [*11*].

The other important factor in the determination of the prevalence rate of carriers in the study was the area of habitation. Other related studies offer conflicting statistics on this point [*8,9,12*]. A study from Nigeria reports that the prevalence of carriers is higher in rural areas [*13*], while another from Nepal states the opposite [*8*]. Living in populated regions is described, in a study from Sudan, as an important determining factor [*14*]. Finally, another study from the United States indicates that living in cities with a population of more than 250 000 has a striking effect on the increase of the carrier prevalence rate. This discrepancy may be due in part to the diverse socioeconomic and sanitary conditions that exist in the villages and cities of various countries. Considering the relatively poor socioeconomic state and sanitary conditions of the villages in the Islamic Republic of Iran, and the absence of certain risk factors in the large cities. such as drug addiction, the growth of urban population has not been regarded as a serious risk factor in the rise of the prevalence rate of carriers: certainly prevalence rates are higher in rural areas.

Hepatitis B infection is considered one of the most important occupational infectious hazards in developed countries [*9*]. Unfortunately, the relationship between career and prevalence of hepatitis in this study was such that finding those most at risk was not possible, and a more specifically designed study would be necessary to obtain data on this goal. However, a statistically significant difference was found in the prevalence rate of carriers among various occupational groups ($P < 0.0001$). However, this observed difference lost its statistical significance when age was eliminated as a confounding factor (i.e. disregarding individuals less than 20 years of age). In addition, the high prevalence of carriers among farmers may be a consequence of their village life, which in turn may also be a variable dependent on other causes.

In general, the main goal of determining those occupational groups at high risk is to take measures to prevent infections in these groups. According to a report by WHO, in the years 1980 to 1985, 6% to 8% of all HBV-infected individuals were hospital personnel. This number decreased to 3% to 4% after a widescale vaccination effort, an illustration of the importance of recognizing the most susceptible occupational groups and of their prompt vaccination [*1*].

Another important factor in the survey was level of education which, without considering the factor of age, had an inverse relationship with the prevalence rate of carriers. It should be noted that the importance of education was maintained even after eliminating age as a confounder. The existence of this relation may be a consequence of direct and indirect relationships of this factor with socioeconomic status, area of habitation, age and other elements which could be pinpointed through more extensive studies.

With respect to marriage and its effects on the prevalence rate of carriers, although the rate of marriage and heterosexual relations is considered a significant risk factor in numerous studies [*15,16,17*], this study showed that the difference in the prevalence rate of carriers between the two groups of never-married and ever-married individuals was the consequence of the age difference between them.

As mentioned above, more than one carrier in a family was observed in one-third of the cases. With a 10% chance of becoming chronic carriers with exposure to the hepatitis B virus, and the exposure of all family members to this infection, this higher rate of prevalence is suggestive of hereditary susceptibility to chronic infection [*18,19*] or a special strain of virus with a higher rate of chronicity. The risk of a child becoming infected was greater when his or her sibling was infected rather than when parents were infected; this is another indication that the mode of transmission is not predominantly vertical. Thus it may be presumed that every member of a carrier's family is exposed to infection and prone to become a carrier, and therefore may be considered high risk. Family members directly exposed to the carrier child were more at risk than those not exposed, having a 9.1% prevalence of HBV markers, while non-exposed family members had a prevalence of 1.7%.

In this study, the youngest subjects were two-year-old children and, as determination of the prevalence rate at or around birth is not possible, an estimation only of prevalence in this group could be made. To obtain such an estimate the prevalence rate of carriers in pregnant mothers was taken as being equal to the prevalence of antigen in the population of women of child-bearing age (15–40 years old), which was equal to 1.6%. A study of 155 healthy carriers of hepatitis B in the Islamic Republic of Iran [*20*] found that 11% of patients were HBeAg positive and 89% were either HBeAg negative or HBeAb positive. In addition, the rate of transmission among HBeAg positives was approximately 90% and among HBeAg negatives or HBeAb positives it was around 10%. From the combination of these two calculations, it was estimated that 18.8% of infants born to carrier mothers were infected with the virus during the perinatal period; 70% to 90% of these infants developed into chronic cases [*21,5*]. Thus, a total of about 0.21% to 0.27% of all infants become chronically infected in the postnatal period. This figure is similar to what has been reported from the Middle East and Africa and suggests that the rate of transmission is low from mother to child (vertical), but occurs most often in the first five years of life and through intimate family contact (horizontal) [*1,5*]. This mode of transmission is different from the methods observed in south-east Asia where vertical transmission (perinatal) plays a major role [*5*]. It is proposed that the reason for this difference is the capability of HBeAg carrier mothers in various communities to transmit the infection.

In general, considering the prevalence rate of HBV carrier in the Islamic Republic of Iran (1.7%) and other data mentioned

above, it seems that the transmission of infection occurs predominantly in children. Approximately half of the subjects were infected between the ages of 10 years and 50 years, indicating that the horizontal mode to transmission is more important than perinatal transmission.

Although the exact mechanism of this transmission is not fully understood, the virus is thought to enter the body through contact with contaminated blood or saliva, through small skin wounds or open sores, but mostly through playmates, sharing objects with others, and family or social contacts. The factor of sex has demonstrated a definite role in the prevalence rate of hepatitis carriers in the survey.

With respect to the history of any disease, no illness had any specific relation with the prevalence rate of hepatitis B carriers. The important point here is that the majority of HBV carriers were asymptomatic.

Conclusion

In the Islamic Republic of Iran, like other countries in the Middle East and north Africa, transmission usually occurs horizontally among young people and in the family environment. It is apparent that vaccination of children under one year of age would be the most logical and effective means of preventing the spread of hepatitis B, as is the case with countries with an intermediate or high prevalence rate. Therefore, the best method is to vaccinate all children under the age of one in accordance with the Expanded Programme on Immunization (EPI). However, in view of the rise in prevalence rates among those between 10 and 50 years of age, and since the Islamic Republic of Iran is an intermediate area and everyone is at risk of acquiring HBV infection, mass immunization is recommended for the population, it being cost–effective in terms of medical costs alone.

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