

# Rate of hepatitis B seropositivity following mass vaccination in the Islamic Republic of Iran

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معدل الإصابة المصلية التالية للتطعيم الجموعي ضد التهاب الكبد البائي في جمهورية إيران الإسلامية

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**الخلاصة:** يتم إجراء التطعيم الشامل لجميع المواليد ضد فيروس التهاب الكبد البائي (بي) في جمهورية إيران الإسلامية منذ عام 1993. ولتقييم كفاءة البرنامج أُجريت دراستان مسحيتان كبيرتان من المسوحات الوبائية المصلية، قبل وبعد التطعيم الجموعي، في عينة ممثلة، شملت واحداً من ألف من السكان. وقد أظهرت معدلات الإصابة المصلية الإجمالية عدم وجود تفاوت يُعتدّ به إحصائياً بين عامي 1991 و1999، اللهم إلا في الفئة العمرية 2 – 14 عاماً حيث نقصت المعدلات بشكل يُعتدّ به إحصائياً (لتصل إلى 0.8% بعد أن كانت 1.3%). ومن الجدير بالذكر أننا لاحظنا نقصاً ملحوظاً أكثر في معدّل حَمَلَة فيروسات التهاب الكبد البائي في المناطق الريفية (0.6% بعد أن كان 1.5%) بالمقارنة مع المناطق الحضرية (0.9% بعد أن كان 1.1%). وهكذا أنقص التطعيم الجموعي معدلات حَمَلَة الفيروس بين صغار الأطفال في هذا البلد بصورة يُعتدّ بها إحصائياً.

**ABSTRACT** Universal vaccination of all neonates against hepatitis B virus has been implemented in the Islamic Republic of Iran since 1993. To evaluate the efficacy of the programme, 2 large seroepidemiologic surveys were conducted before and after mass vaccination on a representative sample of 1/1000 of the population. The overall seropositivity rate showed no significant decline between 1991 and 1999 but in the age group 2–14 years the rates reduced significantly (1.3% versus 0.8%,  $P < 0.05$ ). Interestingly, we observed a significantly higher decline in hepatitis B virus carrier rate in rural (1.5% versus 0.6%) than urban areas (1.1% versus 0.9%). Universal vaccination significantly decreased the carrier rate among young children in this country.

## Taux de séropositivité à l'hépatite B après la vaccination de masse en République islamique d'Iran

**RÉSUMÉ** La vaccination de tous les nouveau-nés contre le virus de l'hépatite B est appliquée en République islamique d'Iran depuis 1993. Afin d'évaluer l'efficacité du programme, deux grandes enquêtes séro-épidémiologiques ont été réalisées avant et après la vaccination de masse auprès d'un échantillon représentatif de 1/1000 de la population. Le taux de séropositivité global n'a pas baissé significativement entre 1991 et 1999 mais dans le groupe d'âge de 2-14 ans, ce taux a diminué significativement (1,3 % vs 0,8 %,  $p < 0,05$ ). Fait intéressant, on a observé une diminution du taux de portage du virus de l'hépatite B significativement plus importante en milieu rural (1,5 % vs 0,6 %) qu'en milieu urbain (1,1 % vs 0,9 %). La vaccination universelle a permis de réduire significativement le taux de portage parmi les jeunes enfants dans ce pays.

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## Introduction

Hepatitis B is one of the most common viral infections in the world. Approximately 350 million individuals are chronically infected carriers of the virus and at high risk of death from active hepatitis, cirrhosis and primary hepatocellular cancer [1]. Each year, approximately 1 million people die from the acute and chronic sequelae of hepatitis B virus (HBV) infection, making it one of the major causes of morbidity and mortality worldwide [2–4]. The HBV carrier rate varies widely from 0.01% to 20% in different geographical regions of the world [5]. The development of safe and highly effective hepatitis B vaccines now provides the means to confer long-term immunity against HBV infection [5–7]. In May 1992, the World Health Assembly, the governing body of the World Health Organization, endorsed recommendations stating that all countries should have hepatitis B vaccine integrated into their national immunization programmes by 1997 [4].

Postnatal horizontal transmission of HBV in early childhood seems to be the predominant method by which high HBV carrier rates in the Middle East are maintained. Infection in the first 5 years of life makes the largest contribution to the caseload of chronic liver disease and thus to mortality from HBV [8]. Mass vaccination programmes to reduce the rate of chronic hepatitis and its carrier state in regions with a high prevalence of HBV infection have been implemented in different parts of the world. The results have been promising, and marked reductions in the carrier rate among children have been reported in follow-up studies [4,9–11]. Even in countries with a low frequency of the disease, the authorities are strongly considering implementing universal immunization programmes as a substitute for the current

ineffective strategy of vaccinating carriers and high-risk individuals [5,12].

It is estimated that over 35% of Iranians have been exposed to HBV and about 3% are chronic carriers, ranging from 1.7% in Fars (a province in the south of the country) to over 5% in Sistan va Baluchestan (the most south-eastern province) [13]. It has been concluded that over 50% of Iranian carriers have contracted the infection perinatally, making this the most likely route of transmission of HBV in our country [13].

In the Islamic Republic of Iran, mass vaccination against HBV infection was begun in 1993. Neonates born after this time were required to be vaccinated using recombinant HBV surface antigen. In this study, we assessed the impact of the mass vaccination programme on the carrier rates of HBV in the Iranian population by comparing the rates before and after the programme began.

## Methods

### Study group

The Health and Disease Survey in the Islamic Republic of Iran was conducted in 2 phases, in 1991 and 1999. These 2 large-scale studies were conducted on a 1/1000 nationwide sample of the Iranian population of all age groups. Families from different geographical areas were selected to take part in the studies. A clustering method was used to perform sampling, with each cluster containing 8 families. 'Family' was defined as 1 or more people living together in a common residence. The families were selected from both urban and rural locations in different geographical areas.

During the first health survey 39 841 individuals were enrolled. The sample size for the second health survey was 46 631.

### Data collection

The Ministry of Health and Medical Education assigned a core coordinating team who discussed the goals of the study and planned its design and conduct. In each province, 1 person was selected as provincial supervisor who was responsible for coordinating the data gathering in that province. Provincial supervisors checked all data before submission to the core coordinating team. Sample collection teams were sent to each province, comprising 2 physicians (1 male and 1 female), 1 technician and 1 person trained in interview techniques and the relevant questionnaire.

Blood samples were obtained from all individuals enrolled in the study and were sent as soon as possible to the central laboratory. Samples were tested for presence of the hepatitis B surface antigen (HbsAg) by immunoassay (Hepanostika®, Biomerieux, Netherlands).

### Statistical analysis

The percentage of the population positive for HBsAg were calculated. Differences between rates were estimated for comparable groups and 95% confidence intervals (CI) were calculated as recommended by Altman et al. [14]. All calculations were performed with SPSS, version 10.05 (SPSS, Chicago, Illinois) and CIs were calculated by the Confidence Interval Assessment Program (CIA, copyright 2000, Trevor Bryant).

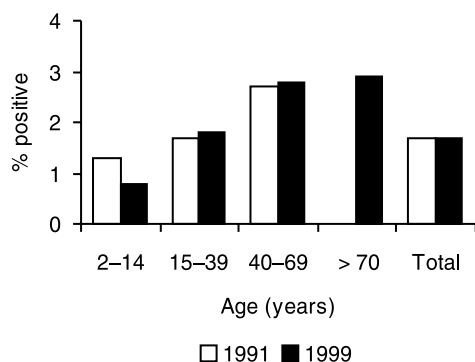
### Results

Among 39 841 individuals tested for HBsAg during the first health survey in 1991, 1.7% (677) had HBsAg detected in their sera (95% CI 1.6–1.8). The HBsAg carrier rate was significant higher in rural

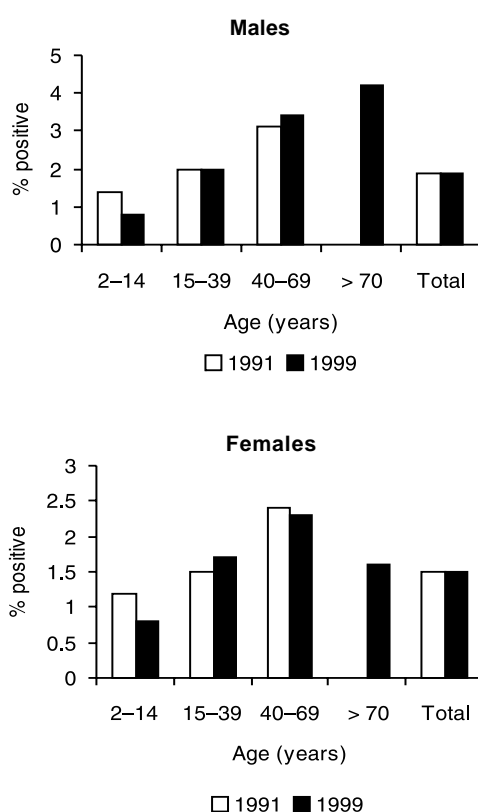
areas (2.0%) than in urban areas (1.5%) ( $P < 0.05$ , 95% CI 0.003–0.008). The HBV carrier rate was 1.5% in females versus 1.9% in males. The difference between men and women was statistically significant (95% CI 0.001–0.006). The age distribution of HBsAg carriers showed that highest prevalence rates were among those aged 30–69 years, while the lowest prevalence (1.3%) was seen among children aged 2–9 years. There was a statistically significant difference of HBsAg carrier state between the age groups 2–14 years old and the rest of the population ( $P < 0.001$ ).

Among 46 631 specimens obtained for screening of HBsAg in the second survey in 1999, 806 (1.7%) were positive (95% CI 1.6–1.9). The rate was 1.8% for urban, and 1.6% for rural areas; this difference was not statistically significant. Women showed a 1.5% rate of positivity and for men this was 1.9%; the difference was significant (95% CI for the difference 0.002–0.006). The carrier rate was 0.8% among children aged 2–14 years old.

Between the first and second health surveys, a significant reduction in HBV carrier rate occurred in children between 2 and 14 years old (1.3% versus 0.8% respectively,  $P < 0.05$ , 95% CI for the difference 0.003–0.007) (Figure 1). This decline was uniformly seen both in males (1.4% versus 0.8%) ( $P < 0.05$ , 95% CI for difference 0.003–0.009) and females (1.2% versus 0.8%) ( $P < 0.05$ , 95% CI for difference 0.001–0.007), but was not observed in other age groups (Figure 2). Decline was more pronounced among children living in rural areas (1.5% versus 0.6%) ( $P < 0.05$ , 95% CI for difference 0.006–0.013) compared with those living in urban areas (1.1% versus 0.9%) ( $P < 0.05$ , 95% CI for difference –0.001 to 0.005) (Figure 3).



**Figure 1 Hepatitis B surface antigen carrier rate in the Iranian population by age, comparing health surveys in 1991 and 1999**



**Figure 2 Hepatitis B surface antigen carrier rate in the Iranian population by age and sex, comparing health surveys in 1991 and 1999**

## Discussion

Our comparison of serum HBsAg positivity rates in the general population of the Islamic Republic of Iran between 1991 and 1999 shows no change in the overall rate of HBsAg positivity. To be more precise, the rate did not change in the age group 15–69 years during this time, while among children aged 2 to 14 years old a significant reduction in HBsAg seropositivity was observed. This result was seen both in male and female subjects and in urban and rural areas.

Interestingly, after the mass vaccination programme the higher rate of HBsAg carriers in rural areas changed to a lower rate compared with urban areas. We speculate that this may be due to the particular design of the health system in rural parts of this country, which is delivered through a special network of health houses. In these houses, health staff prepare a specific record for each family in their village and monitor the vaccination status of any newborn in the area. Vaccinations may be delivered at home if the family lives far from a health house. In urban areas, vaccination provision is more dependent on families attending special facilities that provide such services. The different vaccination delivery systems may explain the more pronounced decline in HBsAg seropositivity rate in 2–14-year-old children living in rural areas compared with those living in urban areas. Although during the first and second health surveys, no data were provided concerning complete vaccination coverage rates, other studies from the Iranian Ministry of Health and Medical Education show that vaccination coverage is overall above 95%. We think our data provide indirect evidence that implementation of mass vaccination against hepatitis B virus may be effective in reducing the hepatitis B carrier rate in the population.

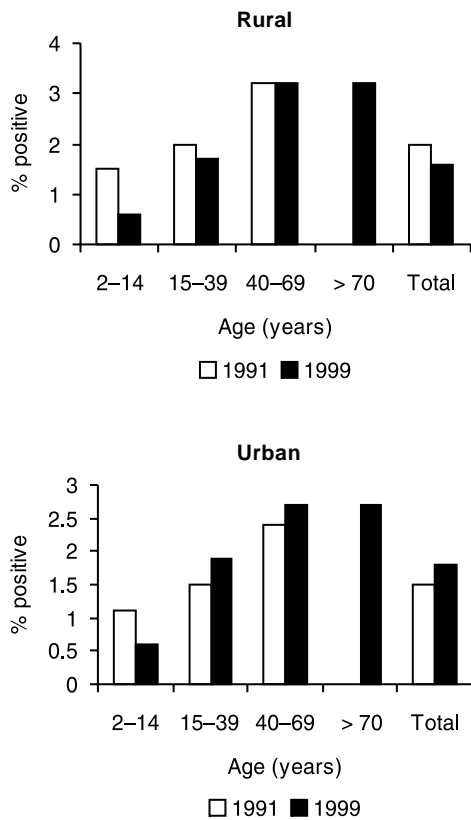


Figure 3 Hepatitis B surface antigen carrier rate in the Iranian population by age and area, comparing health surveys in 1991 and 1999

The universal vaccination programme against hepatitis B was launched in 1993. As the Islamic Republic of Iran is considered a country with an intermediate rate of HBV infection, there will not be a rapid decline in the overall carrier rate, and the rates of chronic liver disease and deaths resulting from HBV are unlikely to change over a period of less than one decade [13,15]. Anyhow, the rate of carrier state among children is a good proxy for evaluating the effectiveness of this programme. Other prevention strategies (such as successive

vaccination of predefined cohorts) may be necessary to deliver a more rapid decline in the hepatitis B carrier rate.

Vaccination has been reported to result in adequate protection in about 90% of cases. Integration of HBV into the WHO Expanded Programme on Immunization for mass vaccination of infants in areas where HBV infection is endemic and morbidity is high would be the most effective means of providing the coverage necessary for effective control and prevention [3]. Following the neonatal vaccination programmes that were begun in 1989 in Saudi Arabia, the overall HBsAg carrier rate in children under 12 years old fell from 6.7% in 1989 to 0.3% in 1997 [16]. Chen et al. [17] showed that 10 years after implementation of mass vaccination in Taiwan, the HBsAg seropositivity rate declined from 9.8% to 1.3%.

Mass vaccination has been shown to be a safe and highly effective means for the control and prevention of HBV [4]. The 2 main challenges to eradication of hepatitis B in the next few decades are, first, the presence of a large worldwide reservoir of carriers that requires a continuous effort to sustain immunization programmes and, secondly, how to make vaccines and drugs available to countries with limited resources [12]. The problem of hepatitis B carriers is of paramount importance as the eradication of hepatitis B can be achieved only after the 300 million carriers of the disease in the world today have died or been cured [18].

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