

Seroprevalence of hepatitis B in Nahavand, Islamic Republic of Iran

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معدل الانتشار المصلي لالتهاب الكبد البائي في نهاوند، جمهورية إيران الإسلامية

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الخلاصة: قام الباحثون بتحديد معدل الانتشار المصلي لالتهاب الكبد البائي في نهاوند في عينة ضمت 1824 شخصاً فوق سن الخامسة في عام 2002. وأجريت لقاءات شخصية معهم كما أخذت عينات دم منهم. وتم تقييم الترابط بين عوامل الاختطار وبين التهاب الكبد البائي باستخدام التحوف اللوجستي. ووجد أن معدل انتشار الحالات الإيجابية لمستضد التهاب الكبد G هو 2.3%؛ وتم استفاد الضد البائي لالتهاب الكبد البائي لدى 11.6% من المشاركين وال ضد السطحي لدى 7.8%. وكان 11.9% من المشاركين إيجابيين لكلا الضدَّين السطحي والبائي. وتبين أن سابقة إجراء عملية جراحية أو التواجد في السجون تمثل أهم عوامل اختطار العدوى بنسبة أرجحية 2.14 (95% فترة الثقة 1.22 - 3.05) للأولى و 3.5 (95% فترة الثقة 1.68 - 5.4) للثانية.

ABSTRACT We determined the seroprevalence of hepatitis B in Nahavand in a sample of 1824 subjects > 5 years in 2002. Face-to-face interviews were conducted and blood samples taken. The association between risk factor and hepatitis B was assessed using logistic regression. The prevalence of HBsAg positive cases was 2.3%, and HbCAb and HBsAb were isolated in 7.8% and 11.6% of the participants respectively; 11.9% were positive for both HbCAb and HBsAb. History of surgery and imprisonment were the major risk factors for infection with odds ratios of 2.14 (95% CI: 1.22-3.05) and 3.57 (95% CI: 1.68-5.4) respectively.

Séroprévalence de l'hépatite B à Nahavand (République islamique d'Iran)

RÉSUMÉ Nous avons déterminé la séroprévalence de l'hépatite B à Nahavand dans un échantillon de 1824 sujets âgés de plus de 5 ans en 2002. Des entretiens face à face ont été menés et des prélèvements sanguins ont été effectués. L'association entre le facteur de risque et l'hépatite B a été évaluée au moyen de la régression logistique. La prévalence des cas Ag HBs positifs était de 2,3 % ; des anticorps anti-HbC et des anticorps anti-HBs ont été isolés chez 7,8 % et 11,6 % des participants respectivement ; 11,9 % étaient positifs à la fois pour les anticorps anti-HbC et les anticorps anti-HBs. Des antécédents de chirurgie et d'emprisonnement étaient les principaux facteurs de risque d'infection, avec un odds ratio de 2,14 (IC 95 % : 1,22 - 3,05) et 3,57 % (IC 95 % : 1,68 - 5,4) respectivement.

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Introduction

The prevalence of hepatitis B worldwide is 5%, which makes it one of the most prevalent infectious diseases. It is estimated that 400 million people in the world are carriers of hepatitis B virus (HBV) with 75% to 80% living in Asia and Eastern Europe [1]. Middle East countries have an intermediate prevalence with 2%–7% infection in the general population and a 20%–60% lifetime risk of infection. Chronic hepatitis B accounts for about 1 million deaths each year and is a major risk factor for cirrhosis and hepatocellular carcinoma [1,2].

In an epidemiological study in the Islamic Republic of Iran, hepatitis B prevalence has been reported to be as low as 1.07% in Shiraz to as high as 8.96% (in Toicerkan). The prevalence in provinces ranges from 1.7% in Fars to 5% in Sistan-o-Baluchestan. In Tehran 3.6% of men and 1.6% of women were reported to be hepatitis B surface antigen (HBsAg) positive [3].

The main route of HBV transmission, like hepatitis C virus (HCV) and human immunodeficiency virus (HIV) is via blood and blood products. In hyperendemic regions in the world vertical transmission from mother to newborn infant and horizontal transmission among children play an important role in intra-familial transmission of HBV [4–6]. In North America and Western Europe, however, the main route of transmission is intimate sexual contact [1]. Needle-stick injuries in health personnel, haemodialysis, shared needles in drug abusers, dental surgery, receiving blood or blood products, blood letting, ear and nose piercing practices, tattooing, and contact with body fluid or mucosa of HBV carriers (e.g. workers in clinical laboratories) have been associated with increased risk of transmission [1].

In the Islamic Republic of Iran, 46% of patients with hepatocellular carcinoma and

51% of those with cirrhosis are reported to be HBsAg positive [7]. HBV is also recognized as the most frequent cause (70%–80%) of chronic hepatitis in the country.

Of all measures to control the disease in the Islamic Republic of Iran, vaccination of all newborns from 1993 onwards has been the most significant. In order to devise any further measures to control this disease more exact epidemiological information is required.

There has been no definitive study about prevalence of hepatitis B in the city of Nahavand in Hamedan province in the western part of the Islamic republic of Iran. Therefore, in this study, we aimed to determine the prevalence of hepatitis B in Nahavand and its associated risk factors.

Methods

This cross-sectional study was conducted during a 2-month period (February–March 2003) on people aged 6 years and over in the city of Nahavand (72 000 population). We used lot quality assurance sampling (LQAS) to select individuals from the general population of Nahavand. Of the 6 urban areas from the health administrative system map in Nahavand, 5 (amounting to over 61 000 people) were included in the study and 1824 participants were recruited through systematic random sampling (approximately 365 participants in each area as a stratum) [8]. The area excluded covered mostly suburban populations. Based on data extracted from the 1999 census registry, the number of potential candidates and their contact address and phone numbers were determined by the family health official of each health care centre.

A questionnaire including demographic and socioeconomic data and risk factors of hepatitis B was developed by gastroenterol-

ogists and epidemiologists at the Research Centre. After taking the approval of health authorities of the city and the city council, training of data collection teams and directors of health care centres was held to train them on conducting the interview, filling the questionnaire and blood sampling.

The selected participants were contacted and interviewed at their homes. If the chosen family was not available due to change of address, refusal or some other reason, another family was selected to replace them using the same sampling procedure. Every participant signed an informed consent form before the interview. For those between 5 and 15 years the consent form was signed by one of the parents. The blood samples and completed questionnaires were gathered at the end of each day. The serum samples were sent to the Research Centre in Tehran to be assessed for hepatitis B serologic markers.

The virologic markers of hepatitis B were measured. HBsAg detection was carried out with a DiaSorin kit (No. 0370790/1A) (DiaSorin, Saluggia, Italy) through sandwiched enzyme-linked immunosorbent assay (ELISA). Levels of antibodies to hepatitis B surface antigen (HBsAb) and hepatitis B core antigen (HBcAb) were measured by DiaSorin kit (No. 9230320/A) through sandwiched non-competitive ELISA and DiaSorin kit (No. 8540480/1B) through competitive ELISA respectively. Hepatitis Be antigen (HBeAg) detection was carried out with a DiaSorin kit (No. 3120128) through sandwiched non-competitive ELISA. HBsAb titres over 10 U/mL were considered positive.

All data were analysed with *SPSS*, version 11. Bivariate and multivariate associations of seropositivity (as binary dependent variable) with other independent variables were examined by logistic regression model, and odds ratios (OR) and correspond-

ing 95% confidence intervals (CI) were calculated.

Results

Of all the selected individuals, 85 (4.6%) did not participate due to change of address or refusal, and were replaced by others who were eligible. The total number of participants over 5 years in the chosen families was 7682. As regards sex, 1025 (56.2%) of the participants were male and 799 (43.8%) were female. Mean age (standard deviation) was 34.8 (SD 19.6) years, range 6–93 years. The age distribution of the participants is shown in Figure 1. The most frequent age group was 15–20 years. The age distribution of our sample was compared with that of the Health Surveillance Study carried out in April 1998 to March 1999 by the National Centre for Medical Research for the whole country [7] (Figure 2).

As regards demographic data, 1005 (55.1%) of the participants were married. The mean size of households was 4.8 (SD 1.9) members, range 1–13 members. The mean number of members over 5 years of age per family was 4.2 (SD 1.9).

The frequency distribution of hepatitis B serological markers in the study participants is shown in Table 1. Of the 1824 participants, 42 (2.3%) were positive for HBsAg. Only 2 of these 42 (4.8%) were aware of having hepatitis B before the results of blood sample tests were revealed. Of the 42 HBsAg positive participants, 4 (9.5%) were also HBeAg positive, indicating wild type condition in these subjects. Among the sample, 13 (7.8%) were positive for HBcAb and 211 (11.6%) were positive for HBsAb; 217 (11.9%) were positive for both HBsAb and HBcAb.

Age frequency distribution of participants with hepatitis B showed that the fre-

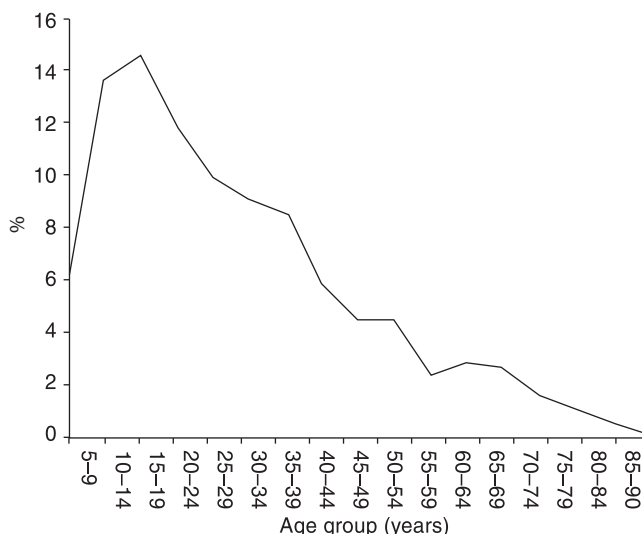


Figure 1 Age distribution of the participants of the Nahavand study (n = 1824)

quency of the disease increased with age with age groups of 55–59 years and 80–84 years having the highest rates of the disease. The disease was not observed in 5–9-year-old participants (Figure 3).

Logistic regression analysis was used to find the risk factors most strongly associated with the disease (Table 2). History of surgery and imprisonment had the greatest risk with OR of 2.14 and 3.57 respectively.

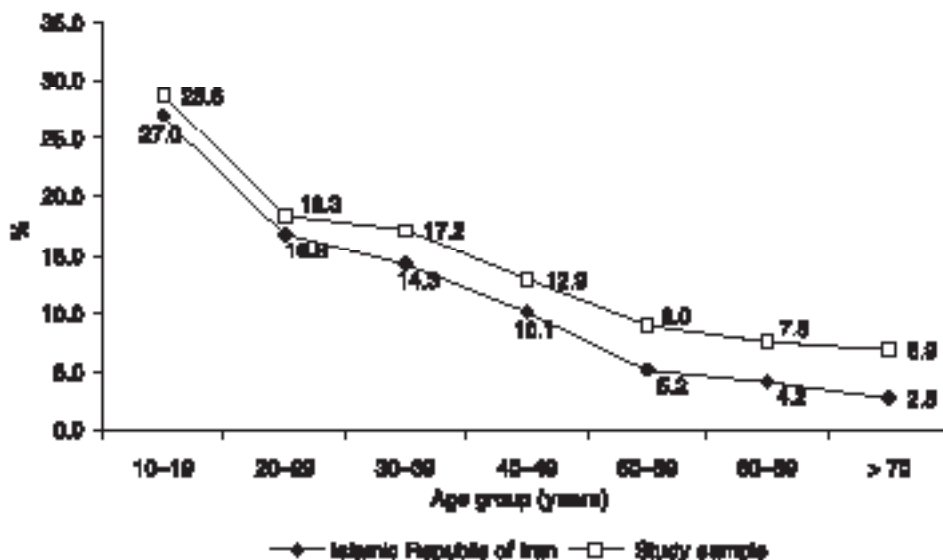


Figure 2 Age distribution of the participants compared with that of the Health Surveillance Study [7]

Table 1 Frequency distribution of hepatitis B serologic markers among the participants of the Nahavand study by demographic variables (n = 1824)

	Positive for HBsAg	Positive for isolated HBcAb	Positive for isolated HBsAb	Positive for HBcAb & HBsAb
No. (%)	42 (2.3)	143 (7.8)	212 (11.6)	217 (11.9)
% male	54.8	44.1	41.5	53.9
Mean age (SD) (years)	40.2 (18)	55.2 (16)	37.3 (22)	52.8 (17)
% married	66.7	71.3	51.4	80.2

SD = standard deviation.

Of all the participants, 5 had thalassaemia major, 6 had renal failure and were undergoing haemodialysis, 2 had haemophilia and 16 had diabetes. However, of these, only 1 diabetic patient had hepatitis B. Being affected with these diseases was not considered in the regression analysis of risk factors to allow a more exact calculation of attributable risk.

Figure 4 shows the proportion of study participants positive for HBsAb according to age group. In the 5–9 years age group, only 33.6% of the subjects had an acceptable level of HBsAb. The proportion of individuals with adequate HBsAb levels increased with age.

Figure 5 shows the proportion of participants positive for HBcAb according to

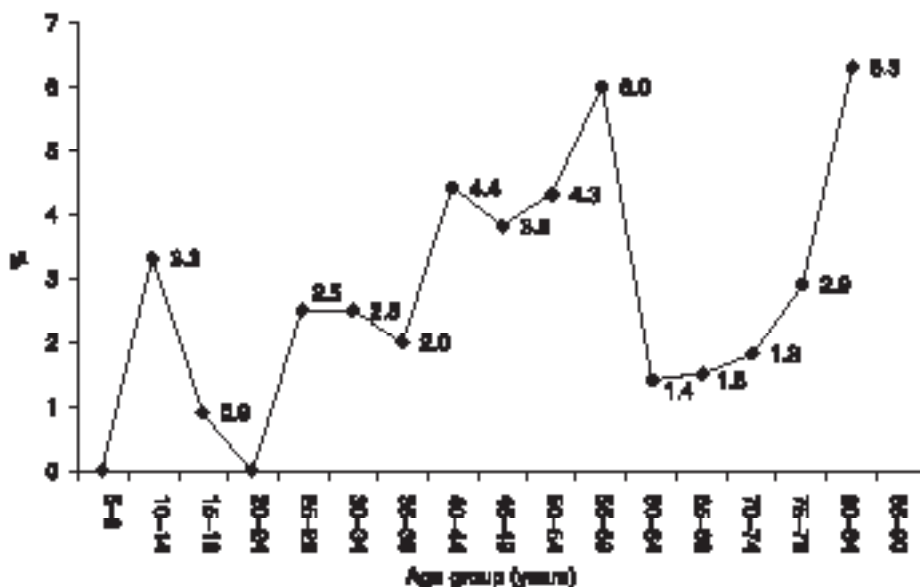


Figure 3 Distribution of HBsAg positive cases among participants according to age group

Table 2 Logistic regression analysis of risk factors for hepatitis B in the study sample

Variable	β coefficient	Odds ratio	Confidence interval	P-value
Sex	0.53	1.71	0.820–2.950	0.1
Age	0.022	1.022	0.900–1.040	0.01
Blood transfusion	0.656	1.92	0.870–3.040	0.399
Tattoo	0.55	1.74	0.930–2.100	0.99
Cupping	-0.28	0.75	0.490–1.510	0.57
Outpatient surgery	0.231	1.26	0.750–1.690	0.54
Smoking	-0.57	0.56	0.300–1.020	0.311
High-risk job	-0.435	0.013	0.003–0.027	0.74
History of jaundice	-0.07	0.92	0.840–1.120	0.94
History of hospitalization	-1.74	0.17	0.006–0.032	0.01
Surgery	1.27	3.57	1.680–5.400	0.062
History of imprisonment	0.76	2.14	1.220–3.050	0.32
History of liver disease in family	0.53	1.71	0.970–2.360	0.21

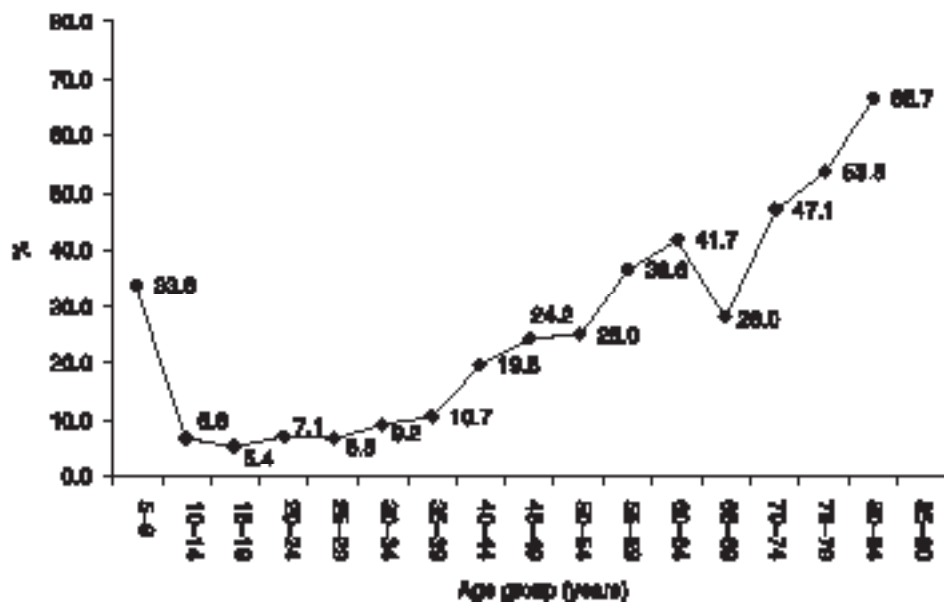


Figure 4 Proportion of subjects positive for HBsAb according to age group

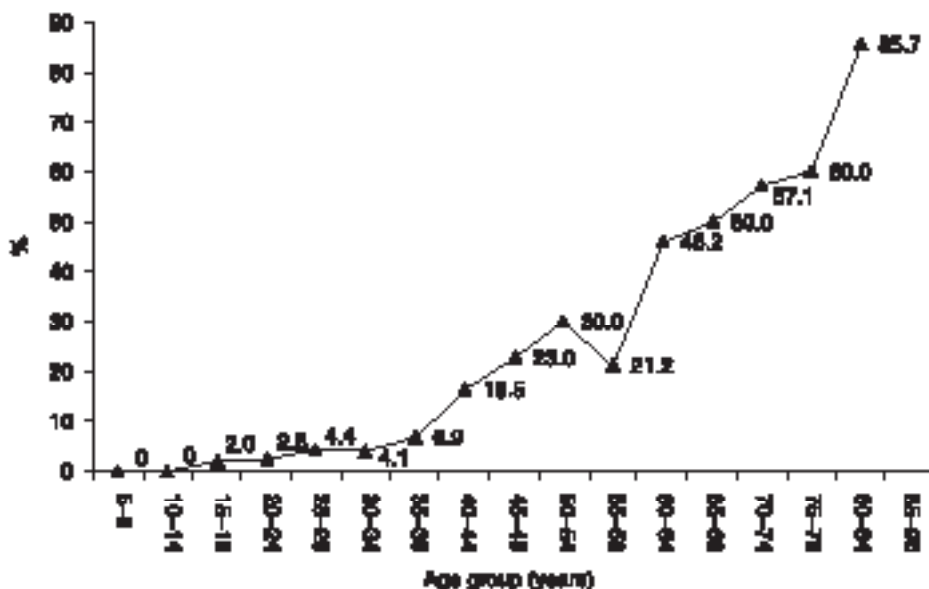


Figure 5 Proportion of subjects positive for HBcAb according to age group

age group. This group represents those who were still affected by the disease. The proportion of participants positive for HBcAb increased with age.

Standardized morbidity rate (SMR) for hepatitis B was 1.3 (95% CI: 0.81–1.53).

Discussion

A comparison of age frequency distribution of the sample and that of National Health Surveillance [7] showed no significant difference which suggests the sample was representative of the respective society.

The prevalence of HBsAg among our sample in Nahavand was 2.3%. Comparing this with national norms of hepatitis B prevalence [7] showed that the standardized morbidity rate (SMR) was 1.3 (95% CI: 0.81–1.53). Based on the calculated SMR and respective CI, there was no significant difference between the prevalence of hepatitis B in Nahavand and national norms.

In a study in 1989 in Hamedan province, 4930 people (1649 men and 3281 women) were tested for hepatitis B risk factors and markers and 3.49% were found HBsAg positive [9]. Of those with HBsAg, 13.8% were also HBcAg positive. The lowest prevalence was observed in children and young adults under 19 years and in those over 60 years. There was no difference between men and women. This study suggested that horizontal transmission of the disease may be the major form of transmission in children and young adults [9]. In our study, the frequency of HBeAg positive cases was 9.5%, clearly lower than that reported by other studies [10,11].

In a study on 11 455 blood donor medical records at a blood transfusion organization of Hamedan in 1995–1996, 1.9% of donors were HBsAg positive [10]. The highest rates (8.69%) were reported from Toicerkan and the lowest from Gharveh (1.3%) and Hamedan (1.36%). The lowest rate

(0.96%) was observed in 58–68 years age group. In another study of 104 236 blood donor records in Hamedan in 1981–1993 (12 years), the overall HBsAg prevalence was 2.96%. Of the HBsAg positive cases, 164 were examined for HBeAg and HBeAb with 82.3% HBeAb positive, 11% HBeAg positive and 6.7% positive for both markers. The disease was most prevalent in farmers, with Nahavand having the highest rate in Hamedan province [11]. In a recent study in Khorasan province, hepatitis B prevalence was 3.6% [12].

In other countries variable prevalence rates of hepatitis B have been reported [13–16]. A study in Bangkok reported a prevalence of 4.6% for HBsAg positive cases with 20% also being positive for HBeAg [14]. Croatia has less than 2% of HBsAg carriers in the general population [15] and a study in Pakistan revealed 2.56% of individuals in the general population were positive for HBsAg [16].

Our results show that there were no cases of hepatitis B in the 5–9 years age group. This suggests that the national vaccination programme has reduced the hepatitis B prevalence, so improving the coverage of vaccination seems necessary. The fact that the rate of HBsAg positive cases increased with age, suggests the critical role of horizontal transmission.

The results of our study show a lower prevalence for hepatitis B in Nahavand than previously reported [10,11]. It is important to note that in the previous studies, the prevalence of hepatitis B was assessed in blood donors who may not be representative of the community. However, in our study the sample was representative of the community.

HBsAb was isolated in 11.6% of our participants, which is likely to be the result of hepatitis B vaccination. A study in 1989 found HBsAb and HBcAb prevalence rates

in Hamedan of 18.09% and 5.13% respectively [9], which are different from our results. The differences could be due to the different times of these studies, different locations and differences in compliance with vaccination.

As regards vaccination status, 44% of the participants reported previous vaccination and 30% were not aware of their vaccination status. HBV vaccination of all newborns began 10 years before our study. So, the subjects under 10 years old must have received HBV vaccine through the national immunization programme. Given the 95% coverage of hepatitis B vaccination and 33.6% prevalence of isolated HBsAb in the 5–9 years age group, the antibody response in children seems inconsistent. A booster dose of hepatitis B vaccine should, therefore, be carefully evaluated. A number of studies have reported antibody response rates. Goldenberg et al. reported a lack of response in up to 14% of adults [17]. In another study on 1–3-year-old Turkish children, 96.7% had an antibody titre of more than 10 U/mL [18].

In our study, 11.9% of the participants were positive for both HBcAb and HBsAb. In a study carried out on 1000 blood donors in Brazil in 2003, 120 had HBcAb; 10 (8.3%) of whom also had HBsAg [19]. All the individuals with HBcAb were positive for HBV DNA, confirmed by polymerase chain reaction (PCR); 2 had HBsAb [19]. In a German study, HBcAb and HBsAb were detected in 1.5% of HBsAg-negative cases; HBV DNA was confirmed by PCR [20]. In another study of Chinese blood donors, no cases of HBV DNA were detected in individuals positive for HBsAb and HBcAb [21]. In a study on 9006 Swiss women, 1.2% had HBcAb and 5.1% had both HBcAb and HBsAb [22]. This is lower than our results.

A history of imprisonment and surgery had the highest attributable risks for hepatic

tis B infection. In the study on blood donors of Hamedan, a history of surgery had the greatest risk (OR = 3.11) for hepatitis B [10]. The risk factors identified in our study are similar to studies carried out in other countries [23].

Nahavand can be classified intermediate in terms of HBsAg prevalence in its

population. Given the result of this study, public health education and vaccination programmes should be continued progressively. We recommend further investigation into the relation between surgery and increased risk of hepatitis B to find effective intervention for reducing the risk of hepatitis B transmission.

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