

## Hepatitis B surface antigen prevalence in pregnant women: A cross-sectional survey in Iran

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### ABSTRACT

**Background:** Vertical transmission of hepatitis B virus (HBV) from infected mothers to their neonates is one of the most important routes of infection. The exact prevalence rate of HBV in Iranian pregnant mothers is not well known but based on different studies it is estimated between 0.35% and 6.5%. The aim of this study was to determine the seroprevalence of hepatitis B surface antigen (HBsAg) in pregnant women of selected provinces in Iran.

**Methods:** At this cross-sectional study, seven provinces supposed to be of high and low prevalence of hepatitis B in the general population selected. Multistage sampling was used to enroll 5261 parturient women who attended the target provinces birth facilities, during January to March of 2011, were recruited to study. To determine the statistically significant mean and proportion differences, *t*-test and  $\chi^2$  test were used, respectively.

**Results:** Overall 1.2% was positive HBsAg of which 11% of them were hepatitis B e-antigen positive as well. The eastern and north eastern provinces were considerably higher in HBsAg seropositivity than the west and northwest of the country.

**Conclusions:** In view of the considerable prevalence of hepatitis B in pregnant women, screening all pregnant women prioritizing the eastern and north-eastern provinces is strongly recommended.

**Keywords:** Hepatitis B, Iran, pregnant women, prevalence

### INTRODUCTION

Hepatitis B is a liver infection caused by the hepatitis B virus (HBV). It is most severe type of viral hepatitis which can lead to chronic liver disease and even death from cirrhosis and liver cancer. According to WHO 2012 report,<sup>[1]</sup> an estimated two billion people have been infected with the HBV and more than 240 million have chronic (long-term) liver infections and about 600,000 people die every year due to the acute or chronic consequences of hepatitis B. Based on the HBV prevalence classification<sup>[2]</sup> Iran can be considered as intermediate endemicity

country of HBV. It is estimated that about 1.5 million people in Iran are living with HBV infection and that 15–40% of them are at risk of developing cirrhosis and/or hepatocellular carcinoma without intervention.<sup>[3]</sup> It is also estimated that 225,000–600,000 individuals are at risk of serious health problems related to HBV infection and need immediate attention. Whereas there are many unknown hepatitis B surface antigen (HBsAg) positive carriers, which may disseminate infection to healthy people.<sup>[3]</sup>

The vertical transmission of HBV from infected mothers to their neonates is one of the most important routes of infection worldwide, however the exact prevalence rate of HBV in Iranian pregnant mothers is not well-known but based on different studies it is estimated between 0.35%, and 6.5%.<sup>[4-7]</sup> The horizontal transmission of HBV to the children in the first years of life is important as well. In the case of infants born to mothers both HBsAg and hepatitis B e-antigen (HBeAg) positive the risk of being infected by the mothers will increase.<sup>[8]</sup> HBV does not transmit through placenta, but the infection occurs during the delivery process.

Mass vaccination of neonates against HBV infection started from 1993 as a national program in routine neonates care in Iran. This program is supposed to affect the prevalence rate of HBV infection through the country and decrease the rate of infection after a while.<sup>[9,10]</sup> Despite the good coverage of HBV vaccination, the potential transmission risk of infection from mother to child remains unknown. Therefore, the cost efficiency of HBsAg prenatal screening in Iran is an important concern. Currently, Iranian pregnant women are asked for the history of risky behaviors within their first visit of antenatal care and are referred for HIV and HBsAg test if they are recognized susceptible as carriers. Whereas the effectiveness of the pregnant women risk assessment is under question, the dilemma is whether the HBV prevalence in pregnant women is high enough to convince family health policy makers for routine screening of all pregnant mothers who are attending antenatal care clinics in Iran. Since there was not enough evidence in hand to help decisions on HBV screening in maternal hood, this study was designed to give a better image of the prevalence of HBV in pregnant women in Iran.

## METHODS

At this cross-sectional study, three provinces of Sistan and Baluchestan (S and B), Golestan, Kerman (Jiroft as one of this province districts) and also four provinces of East Azerbaijan, Zanjan, Kurdistan and Lorestan were selected as areas supposed to be of high and low prevalence of Hepatitis B among general population in Iran, respectively.<sup>[3]</sup> Overall, these provinces composed 20% of Iranian population and 24% of total deliveries with live birth. About 67% of married females in mentioned provinces were in childbearing ages (14–45), and more than 95% of labors were carried out in health care facilities.

Multistage sampling was used to enroll participants in two steps. In first step, quota sampling method was used and according to child birth statistics in past year (provided by Iranian Census Organization); the proportion of monthly deliveries for each of the selected provinces was determined. In second step, availability sampling method was used and 5261 parturient women, who attended the target provinces birth facilities, during January to March of 2011, were recruited to study.

Pregnant women who did not declare their written consent were excluded from the study. Participants were interviewed about demographic characteristics, prior medical history, and high-risk behaviors along with 5 cc venous blood sample were obtained by trained staff after transferring mothers to the maternity ward. All the blood samples were centrifuged and frozen.

### Laboratory assessment

All of the collected frozen blood samples were sent to Zanjan Mousavi Central Teaching Hospital Laboratory under standard cold chain. The sera were tested for HBsAg and HBeAg using nine immunochromatography kits of Guangzhou Wandfo Biotech Capital China trademark. Finally, all HBsAg positive sera and 15% of HBsAg negative samples (randomly selected) were rechecked by ELISA commercial kits of Bioelisa, HBsAg 30 (Biokit, S.A. Barcelona, Spain).

### Data analysis

The HBsAg positive seroprevalence and subsequently positive HBeAg with 95% confidence interval (CI) were determined in seven selected provinces. To determine the statistically significant

mean and proportion differences, *t*-test and  $\chi^2$  test were used, respectively. As dependent variable, the HBsAg status was split into two categories (positive-negative) and association of seropositivity and common HBV infection risk factors as socio-demographic characteristics, obstetric history, and high-risk behaviors were tested by odds ratio.

## RESULTS

Overall 64 cases out of 5261, were positive HBsAg among screened pregnant women (prevalence rate: 1.2%, 95% CI: 0.9–1.5), including seven HBeAg-positive (prevalence rate: 11%, 95% CI: 5–20). As presented in Table 1, the prevalence rate of HBsAg-positive seromarker was different in seven provinces. Jiroft, Golestan and S and B had contributed to high seropositivity rates of HBsAg and HBeAg.

The majority of Jiroft, Golestan and S and B subjects were multigravida with a history of stillbirth and abortion statistically significant (67% vs. 57% and 66% vs. 18%,  $P < 0.05$ , respectively), in comparison with the provinces: East Azerbaijan, Zanjan, Kurdistan and Lorestan (data not shown).

Table 2 shows the univariate analysis of baseline maternal risk factors with respect to HBsAg status. Considering age-specific prevalence rate, the age group 37 years and over had the highest rate of positive HBsAg prevalence. However, the difference was not statistically significant ( $P > 0.05$ ). Despite higher proportion of HBsAg seroprevalence

among illiterate groups, there was no significant association between educational level and HBsAg seropositivity ( $P > 0.05$ ). In the case of obstetric history, the positive HBsAg marker was more frequent among pregnant women with gravidity and parity number of four and over, but it was not statistically significant ( $P > 0.05$ ). The subjects without any history of abortion (as a reference group) had the lowest frequency of HBsAg seropositivity. Despite the increased odds of positive HBsAg in concordance to the increase of abortion numbers, the difference was not significant ( $P > 0.05$ ).

Table 3 presents the results of HBsAg status based on selected risk factors. Although the higher proportion of positive HBsAg was detected among those with a history of spotting, there was no statistically significant effect on HBsAg seropositivity (2% vs. 1.15% and  $P > 0.05$ ). Of the 64 positive HBsAg cases, none had a history of IV-drug abuse and imprisonment. However, proportion of HBsAg seropositivity were slightly higher among women whose spouses had a history of substance abuse while difference was not statistically significant (1.4% vs. 1.2% and  $P > 0.05$ ). In addition, spouse prison history and IV drug abuse were not found as significant determinants of HBV infection risk factors.

## DISCUSSION

In this study 5261 pregnant women of seven provinces in Iran were tested for HBsAg positivity. HBV prevalence among tested cases was 1.2%. The frequency of HBsAg + cases was widely variable in different provinces in Iran from 0.0% in Zanjan to 2.3% in Jiroft (Kerman). The difference in the prevalence of positive HBsAg in pregnant women of the studied provinces can be associated with the overall prevalence of hepatitis B among the general population. As seen in the current study, the prevalence of Hepatitis B was considerably higher in the provinces located at the east and northeast of the country, that is, Jiroft, S and B and Golestan. Other studies also indicate more or less similar trend in the prevalence of positive HBsAg mothers in different provinces of the country, that is, 0.35% in Kashan (2002),<sup>[5]</sup> 1.3% in Rafsanjan (2003),<sup>[6]</sup> 2.3% in Kerman<sup>[11]</sup> and 6.5% in Zahedan (2002)<sup>[12]</sup> while at least two other studies done in the districts of Eastern Azerbaijan which is located at northwest

**Table 1:** Prevalence rate of HBsAg seropositivity in pregnant women of seven selected provinces, Iran

District	95% CI	
	HBsAg+prevalence (%)	HBeAg+prevalence (%)
Jiroft (Kerman)	2.26 (1.19-4.25)	33.3 (12-65)
Golestan	1.93 (1.13-3.28)	7 (1.3-33.3)
S and B	1.83 (1.24-2.7)	12 (4.1-29.9)
East Azerbaijan	0.87 (0.49-1.56)	0
Kurdistan	0.77 (0.3-1.98)	0
Lorestan	0.29 (0.08-1.08)	0
Zanjan	0	0

CI=Confidence interval, HBsAg=Hepatitis B surface antigen, HBeAg=Hepatitis B e-antigen

**Table 2:** Seroprevalence of positive HBsAg among pregnant women based on demographic and previous maternal characteristics

	HBsAg status		OR (95% CI)
	Positive (n=64) (%)	Negative (n=5197)	
Age groups			
≤18	5 (1.3)	379	Constant
19-27	27 (1.0)	2655	0.77 (0.29-2.01)
28-36	23 (1.3)	1814	0.96 (0.36-2.54)
≥37	9 (2.5)	349	1.95 (0.64-5.88)
Education			
Illiterate	14 (1.42)	966	Constant
Primary-secondary school	33 (1.29)	2520	0.9 (0.48-1.69)
Diploma	10 (0.84)	1180	0.58 (0.25-1.32)
University	7 (1.3)	531	0.9 (0.36-2.26)
Number of gravidity			
1	25 (1.2)	1996	Constant
2-3	25 (1.05)	2355	0.84 (0.48-1.48)
≥4	14 (1.62)	846	1.32 (0.68-2.55)
Number of parity			
1	42 (1.3)	3088	Constant
2-3	12 (0.68)	1732	0.5 (0.26-0.97)
≥4	10 (2.58)	377	1.95 (0.97-3.91)
Number of abortion			
None	31 (0.1)	3079	Constant
1	19 (1.4)	1322	1.42 (0.8-2.52)
2	13 (1.7)	740	1.73 (0.9-3.32)
3	1 (1.8)	56	1.76 (0.23-13.11)

CI=Confidence interval, HBsAg=Hepatitis B surface antigen, OR=Odds ratio

of the Iran (2.5% Malekan [2006],<sup>[13]</sup> 3.2% Bonab<sup>[14]</sup>) show higher prevalence rate than our study. One reason can be attributed to endemicity of the Hepatitis B in some areas, another reason might be that the high prevalent provinces or districts are less developed and may have poor access to the health services, however we don't have additional evidence to support this idea.

A number of studies available in the region also indicate different figures ranging from 1% Qatar, 1.5% Emirates, 2.1% Turkey,<sup>[15]</sup> 2.5% (2002),<sup>[16]</sup> and 1.6% (2008) Saudi Arabia<sup>[17]</sup> to 5.6% in Sudan (2007)<sup>[18]</sup> and 7.1% Oman (2000).<sup>[19]</sup> An important restriction in this regard is the objectives of the above-mentioned studies and type of sampling, which may be different and seriously affect the results.

In our study, 10.9% of positive HBsAg pregnant women were HBeAg positive too, ranging from 0.0% in Kurdistan to 33.3% in Jiroft (Kerman). This marker was reported 0.00% in two Iranian

studies done in Ahvaz (2004)<sup>[20]</sup> and Qazvin (2001)<sup>[21]</sup> and 0.7% in a study in Lorestan (2007–2008),<sup>[22]</sup> 12.5% in Northern Turkey (2003–2004),<sup>[14]</sup> 0.15% in Saudi Arabia pregnant women (2002)<sup>[15]</sup> and 0.5% in Oman pregnant women (2000).<sup>[13]</sup>

The results of our study did not show any statistical relationship between HBsAg seropositivity and variables such as age, education, gravidity, parity, and abortion history in the studied pregnant women.

Similarly, no relationship was found between HBsAg seropositivity and risk factors such as substance abuse (fumigation or injective) and the imprisonment history of pregnant mothers or their spouses.

Other findings of the current study showed that tattooing and body piercing were not significantly different with HBsAg seropositivity in studied subjects.

An overview of the studies available indicated a wide range of findings in alignment and

**Table 3:** Comparison of HBsAg - positive prevalence rates by HBV infection risk factors in pregnant women

	HBsAg status		OR (95% CI)
	Positive (n=64) (%)	Negative (n=5197)	
Spotting			
No	56 (1.15)	4806	Constant
Yes	8 (2)	391	1.75 (0.83-3.7)
History of substance abuse and drug injection			
No	64 (1.2)	5224	Constant
Yes	0	37	-
History of imprisonment			
No	64 (1.2)	5256	Constant
Yes	0	5	-
Spouse substance abuse history			
No	58 (1.2)	4748	Constant
Yes	6 (1.4)	410	1.19 (0.51-2.79)
Spouse prison history			
No	62 (1.22)	5000	Constant
Yes	2 (1.21)	164	0.98 (0.23-4.05)
Unknown	0	33	-
Spouse IV drug abuse			
No	64 (1.2)	5215	Constant
Yes	0	13	-
Unknown	0	33	-

CI=Confidence interval, HBsAg=Hepatitis B surface antigen, OR=Odds ratio, IV=Intravenous, HBV=Hepatitis B virus

nonalignment of our above mentioned results (with regard to the statistical relationship between Hepatitis B seropositivity with demographic variables and high risk behaviors in pregnant women).

## CONCLUSIONS

Although neonates vaccination against Hepatitis B has been started since 1993, and several studies show a relative decline in its prevalence in the community, but our study revealed a considerable prevalence of Hepatitis B among pregnant women especially those who are residing in east and northeast parts of Iran. Given the findings of this study, laboratory-based screening of all pregnant women prioritizing the eastern and north-eastern provinces is strongly recommended.

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