

Association of Risk Factors With Hepatitis B Surface Antigen Positivity in Pregnant Women at Aga Khan University Hospital Karachi

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ABSTRACT

Objective: To determine association of risk factors with hepatitis B surface antigen positivity in pregnant women.

Study Design: Case control study.

Place and Duration of Study: Two years from 2004 to 2006 at Agha Khan University Hospital.

Materials and Methods: A total of 210 subjects including 35 cases and 175 controls were enrolled into study. A detailed history from study subjects was recorded on a performa during antenatal visits. Univariate and multivariate analysis was done using SPSS package.

Results: A significant association was observed for the history of at least four injections for minor illnesses in past one year (adjusted odds ratio (AOR) = 5.5; 95% confidence interval (CI): 1.6, 18.1) and history of blood transfusion (AOR= 6.025; 95% CI: 2.1, 17.1), with HBsAg status of pregnant women.

Conclusion: We recommend interventions to improve injection safety and to discourage unnecessary therapeutic injections. There is also urgent need for strict enforcement of regulations for safe blood transfusion. Further research is required to estimate proportion and to evaluate reasons for unnecessary injections in women of reproductive age.

Key Words: *Blood transfusion, Therapeutic injections, Parity, Hepatitis B surface antigen*

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Introduction

An estimated 2 billion people are infected with HBV worldwide, among them 350 millions are hepatitis B surface antigen (HBsAg) positive. HBsAg positivity in Pakistan studies selected groups have shown variable prevalence of chronic infection with HBV as assessed by HBsAg positivity: 7% in health professionals, 2%14% in blood donors.¹In developed countries varies from 0.6 percent in Wales, England, to 1.2 percent in Texas, USA.¹ However, higher prevalence of infection with HBV have been reported from various parts of the developing world including 3.5% in Gaza, Palestine², 1.6%7.7 % in Brazil, 19.6 % in Egypt and 2%10 % from various parts of India.³ Pre-employment screening revealed 2.6% HBsAg positivity among the healthy individuals in northern Pakistan⁴ Moreover, some hospital-based studies have

revealed that 30% 42% of the cases of chronic liver disease⁵ and 78% of the cases of hepatocellular carcinoma were positive for HBsAg. Intravenous drug use, needle stick injuries, haemodialysis, tattooing and multiple sexual partners have been identified as common modes of HBV transmission in the developed world.⁶ In many developing countries however, the relative contributions of various routes of HBV infection have not been defined in population-based studies. Due to a lack of universal and appropriate blood screening in these countries, the risk of post-transfusion HBV infection is still unknown.¹ Parenteral routes implicated as the most likely factors for HBV transmission include un-sterilized needles and syringes in health-care settings.^{7,8} Moreover, in low socio-economic settings, horizontal transmissions of HBV through contact with infected family member have also been reported⁹, but these findings are yet to be verified. Developed countries have been successful in reducing the risk of HBV spread by interrupting some of the known routes of HBV transmission

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and through mass HBV vaccinations. The vaccine against HBV infection is available in most of the developing world including Pakistan, but its high cost limits the widespread use. Recently, Pakistan initiated universal HBV vaccination for neonates through its expanded program of immunization with the assistance of Global Alliance for Vaccines and Immunization. However, public health benefits of this initiative require some time to accrue as the program focuses on neonates only.¹ A better understanding of the mode of spread of HBV will help in prevention of HBV infection. No local studies are available about spread of HBV infection in pregnant women. Routine antenatal screening for hepatitis B and C is recommended by the ACOG as well as the RCOG and ensures proper care when positive cases are discovered.¹⁰

This study aimed to identify the risk factors for hepatitis B surface antigen positivity among pregnant women.

Materials and Methods

The study was conducted in outpatient department of Obstetrics and Gynecology at Aga Khan University Hospital, Karachi over a period of Two years from 2004 to 2006. Sample size consisted of 210 subjects. Thirty-five registered pregnant women diagnosed as hepatitis B surface antigen positive were selected as cases. Against each case, five age-matched controls were selected. The inclusion criteria were pregnant women registered in outpatient department of Aga Khan University Hospital who were diagnosed hepatitis B surface antigen positive. Inclusion criteria for controls group were pregnant women registered in outpatient department of Aga Khan University Hospital who were diagnosed hepatitis B surface antigen negative. Those who refused for consent and lost for follow after enrollment into study

before completion of history taking were excluded from study. The demographic characteristics were Age, Area of Residence, Religion, Education, Occupation, Gravidity, Parity, History of previous surgery, History of at least four injections for minor illnesses in past one year, History of blood transfusion. Seven thousand pregnant women registered in outpatient department of Aga Khan University Hospital during the study period were tested for hepatitis B surface antigen as per hospital protocol. Five ml blood was drawn from each pregnant woman. Test was performed by kit second generation by MEIA. Test results were reported as hepatitis B surface antigen positive and hepatitis B surface antigen negative. Thirty-five pregnant women who were diagnosed hepatitis B surface antigen positive were selected as cases. For each case, five age matched pregnant women diagnosed hepatitis B surface antigen negative were selected as controls. Age of the five controls taken against each case was equal to age of that case in year's \pm three years. Study subjects were explained about the study and an informed verbal consent was taken. A detailed history was taken from study subjects in optimal privacy. History was recorded on a predesigned performa. The data were entered and analyzed through statistical package for social sciences (SPSS 16).

Descriptive statistics were computed for area of residence, religion, education, occupation and gravidity among cases and controls by computing their frequencies for the two groups (cases and controls).

Univariate analysis was performed to evaluate the association of each potential risk factor with hepatitis B surface antigen. For each potential risk factor an odds ratio and 95% confidence interval were computed by simple logistic regression method.

Multivariate analysis was performed to study the association of risk factors with

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hepatitis B surface antigen while adjusting for other independent variables. Those variables with a p-value of = 0.20 in univariate analysis were considered for multivariate analysis. Variables found not significant i.e. p-value > 0.05, were removed from the final model. Adjusted odds ratios and their 95% confidence intervals were calculated to present the results of final model..

Results

Thirty-five registered pregnant women diagnosed hepatitis B surface antigen positive were enrolled into study. We also recruited 5 age matched controls for each case from the same outpatient department. Finally we had one seventy five controls for analysis.

Most of the cases (91.4%) and controls (94.9%) were from Karachi.

Islam was the main religion both among the cases (91.4%) and the controls (96.0%).

An equal proportion of cases and controls were Matric and above (82.9%), while 11.4% of cases and 13.1% of controls had education below Matric. Another two percent of cases and seven percent of controls were illiterates as shown in table I.

Many of the cases (62.9 %) and controls (74.9 %) were found to be housewives. Only a small number of cases (2.9 %) and controls (5.7 %) were healthcare workers.

On univariate analysis cases were more likely to have history of at least four injections for minor illnesses in past one year (odds ratio (OR) = 5.5; 95% confidence interval (CI): 1.9-15.8; p-0.002). Similarly history of blood transfusion was found to have significant association (OR=6; 95%CI: 2.3-15.6; p-<0.001) with HBsAg positivity among pregnant women. Education, occupation, parity and history of previous surgery were not found to have significant association with HBsAg status of pregnant

women in this study as shown in table II. Multivariate analysis was used to control the effects of various risk factors on hepatitis B surface antigen status of pregnant women. At multivariate level only two risk factors i.e. history of at least four injections for minor illnesses in past one year and history of blood transfusion, were found significant as shown in table III. The cases were significantly more likely than controls to receive at least four injections for minor illnesses in past one year (adjusted odds ratio (AOR) = 5.5; 95% CI: 1.7-18.1) when adjusted for history of blood transfusion. Similarly cases were more likely to receive blood transfusion in the past (AOR= 6.0; 95% CI: 2.1-17.1) when adjusted for history of at least four injections for minor illnesses in past one year. P-value was <0.001 for both of these factors after adjusting for each other.

Discussion

This study was conducted to determine

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Table I: Distribution Of Demographic Variables Among Cases And Controls

Variables	Cases (n = 35)		Controls (n = 175)	
	n	%	n	%
Area of residence				
Karachi	32	91.4	166	94.9
Outside Karachi	3	8.6	9	5.1
Religion				
Islam	32	91.4	168	96.0
Hinduism	2	5.7	5	2.9
Christianity	1	2.9	2	1.1
Others	0	0.0	0	0.0
Occupation				
House wife	22	62.9	131	74.9
Non healthcare worker	12	34.3	34	19.4
Healthcare worker	1	2.9	10	5.7
Education				
Illiterate	2	5.7	7	4.0
Below Matric	4	11.4	23	13.1
Matric & above	29	82.9	145	82.9
Gravidity				
Primigravida	4	11.4	50	28.6
Multigravida	31	88.5	125	71.4

Table II: Univariate Analysis Showing The Association Of Various Risk Factors With Hepatitis B Surface Antigen Positivity In Pregnant Women By Their Odds Ratios (or) And 95% Confidence Intervals (ci)

	Risk factor	Cases (n = 35)	Controls (n = 175)	Odds ratio	95% CI	P-value
Education	Matric & above	29(82.9%) 4(11.4%) 2(5.7%)	145(82.9%) 23(13.1%) 7(4%)	1 0.9 1.4	0.2 ,2.8 0.3 ,7.2	0.88
	Below Matric Illiterate					
Occupation	Non-health care worker	12(34.3%)	34(19.4%)	1		0.16
	House wife	22(62.9%)	131(74.9%)	2.06	0.9, 4.5	
	Health care worker	1(2.9%)	10(5.7%)	0.57	0.1, 4.7	
Parity	Nulliparous	7(20%)	55(31.4%)	1		0.22
	Para 1-3	25(71.4%)	111(63.4%)	1.9	0.7, 5.1	
	Para >3	3(8.6%)	9(5.1%)	4.6	0.6, 37.5	
History of previous surgery	No	16(45.8%)	99(56.6%)	1		0.23
	Yes	19(54.8%)	76(43.4%)	1.6	0.7, 3.3	
History of at least 4 injections for minor illness in past 1 yrs	No	26(74.3%)	163(93.1%)	1		0.002
	Yes	9(25.7%)	12(6.9%)	4.7	1.9,15.8	
History of blood transfusion	No	23(65.7%)	159(90.9%)	1		<0.001
	Yes	12(34.3%)	16(9.1%)	6.0	2.3, 15.6	

Table III: Multivariate Logistic Regression Analysis of Risk Factors Associated With Hepatitis B Surface Antigen Positivity In Pregnant Women.

Risk factor		Cases (n = 35)	Controls (n = 175)	Odds ratio	95% CI	Adjusted OR	95% CI
History of at least 4 injections for minor illness in past 1 yrs	No	26	163	1		1	
	Yes	9	12	5.5	1.9,15.8	5.5	1.7, 18.1
History of blood transfusion	No	23	159	1		1	
	Yes	12	16	6.0	2.3, 15.6	6.0	2.1, 17.1

$\chi^2 = 26.36$; $df = 2$; p -value < 0.001

association of various risk factors with HBsAg positivity in pregnant women. History of at least four injections for minor illnesses in past one year was significantly associated with hepatitis B surface antigen positivity in pregnant women in this study. Other studies conducted in developing countries have also identified therapeutic injections as a risk factor for HBV infection.^{1,11,12} In developing countries, a

large proportion of patients prefers injectable medicines and considered them more efficacious than other routes of drug administration.¹³ In addition to patients' preference for injection, physicians' prescribing practices, their belief in better efficacy of injected drugs, direct observation of the prescribed therapy, patients demand and financial incentive have been reported as the reasons for increased frequency of injections in developing countries.¹⁴ In Pakistan, the proportion of injections per prescription is one of the highest compared to some other countries.¹³ In a periurban community in Pakistan, women of reproductive age had been found five times more likely than similarly aged men to receive more than ten injections per year during 1994.⁸ In Pakistan a large proportion of injections given for minor illnesses were found unnecessary.^{8,15} In our study injections received for minor illnesses not requiring hospitalization were recorded in order to emphasize the association of HBV transmission with unnecessary use of therapeutic injections. History of blood transfusion was also found significantly associated with HBsAg positivity in pregnant women in this study. Association of blood transfusion with HBV infection had been seen in other studies.^{16,17}

Implementation of stringent donor eligibility criteria, improved donor screening and more sophisticated as well as sensitive methods of antibody, antigen and viral genome detection, have virtually eliminated transfusion transmitted infections in developed countries. The risk of HBV transmission by blood transfusion in the USA was estimated by the Retrovirus Epidemiology Donor Study (REDS) as

1:63,000 units transfused.¹⁸ Screening for HBsAg before blood transfusion is not universal in developing countries including Pakistan. The main source of blood in Pakistan is from replacement donors. Prevalence of HBsAg, HCV antibody and HIV antibody was found much lower in voluntary non-remunerated blood donors as compared to replacement donors in northern Pakistan.¹⁹ In a study conducted in Karachi the practices of most blood banks were found well below WHO standards.²⁰ Occupation was not significantly associated with HBsAg status in this study. Increased rate of blood borne infections among healthcare workers have been well described in the industrialized countries. However the extent of the problem in developing countries has been poorly quantified. Among healthcare workers up to 9% in Pakistan have been reported as HBsAg positive. The prevalence of HBV infection among health care workers is likely to decrease with the implementation of HBV vaccination.²¹ Education; parity and history of previous surgery were not significantly associated with HBsAg positivity among pregnant women in this study. These results are in accordance with the results of previous studies.^{16, 22, 23} Re-call bias is an inherent limitation of a case control. This might have been introduced in measurement of some of the variables especially when past history of injections were exposed. For economic reasons we were unable to test for some other markers of active HBV infection such as HBV DNA and/ or hepatitis B e antigen (HBeAg), and IgM anti-HBc an indicator of early acute HBV infection. Therefore some pregnant women in this category may have been missed since some patients with acute self limited primary HBV infection never have detectable HBsAg in the blood. In the case-control arm of the study, we did not test

controls for anti-HBs (antibodies to HBsAg) to exclude those who might have resolved past infection, became immune and lacked potential to become case as defined in this study. Ascertainment of control's serostatus may have non-differentially led to controls who are not susceptible to HBV infection due to previous infection or immunization, thereby biasing results toward the null. Future studies should take this aspect into account.

Conclusion

We recommend interventions to discourage the use of unnecessary therapeutic injections. Resources and efforts should be invested to educate health care providers as well as the health seekers on hazards and indications of injections in order to reduce injection frequency. Further research is needed to estimate the proportion and to evaluate reasons for unnecessary injections in women of reproductive age. The association of blood transfusion with HBsAg positivity indicates that there is failure to meet standard safety practices in our blood banks. Efforts should be invested to increase awareness among women of reproductive age about mode of spread of hepatitis B.

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