RESEARCH NOTE

HEPATITIS B INFECTION IN BANGLADESHI MOTHERS AND INFANTS

A de Francisco[1], AJ Hall[2], N Alam[1], S Hawkes[1] and T Azim[3]

[1]Public Health Sciences Division, [3]Laboratory Sciences Division, International Center for Diarrheal Diseases Research, Bangladesh; [2]Infectious Diseases Epidemiological Unit, London School of Hygiene and Tropical Medicine, UK

Abstract. In order to estimate the relative importance of perinatal transmission of hepatitis B in rural Bangladesh a cross-sectional study was carried out. Paired-serum samples of infants aged 2-8 months old, a group of new born, and their mothers were tested for hepatitis B markers using a commercial ELISA test kit. In total, 107 (32.4%) positive for HBcAg, 18 (5.4%) for HBsAg, and 4 (1.2%) for HbeAg. Of the infants, 35 (10.5%) positive for HBcAg, 1 (0.3%) for HBsAg, and none for HBeAg. Of the 18 HBsAg positive mothers, 4 (22%) were HBeAg positive. All 14 children of mothers who were HBeAg negative were negative for HBsAg. Only one out of four (25%) of children of HBeAg positive mothers were HBsAg carriers (8 months old), and in three children transmission did not occur (two 8 months, one 6 months old). This survey indicates that hepatitis B is prevalent in rural Bangladesh and that the perinatal transmission mode may be relatively low.

INTRODUCTION

Hepatitis B infection is a major public health problem as it can lead to chronic liver disease and primary liver cancer resulting from chronic carriage of the virus. The transmission of this infection occurs at three stages of life: (i) perinatally from an infectious carrier mother to her child; (ii) horizontally from child to child (the major route of transmission at this age is not known); (iii) sexually and blood-borne, such as through contaminated needles in adolescent and adult life (Hall, 1994). The age at infection is critical because of its influence on the probability of carriage. Children infected perinatally have a 70-90% chance of becoming carriers; those infected in the first four years of life have a 30% chance, and those infected later have less than a 10% chance of becoming carriers (Edmunds *et al*, 1993). The pattern of hepatitis B infection in Bangladesh is unclear although previous reports document an intermediate level of endemicity with adult carriage rates varying from 5.5 to 23% of the population (Islam 1984; Mustafa *et al*, 1986; Zaman *et al*, 1995; Sattar *et al*, 1996). We therefore took the opportunity to analyse paired mother and infant sera for hepatitis B markers of infection. These sera had originally been collected to examine decay in measles antibody levels (de Francisco *et al*, 1998).

MATERIALS AND METHODS

The study was conducted in Matlab, a rural area of Bangladesh located approximately 70 km from the capital Dhaka. Infants aged 2 to 8 months were selected randomly from the demographic surveillance system (4 children from each of 80 areas) and blood samples were collected by venipuncture. In addition, cord blood was collected from 33 consecutive children born at the Matlab Hospital. Assays were conducted in Dhaka blindly to obtain information from the sample source, but mother and infant pairs were analysed in the same batch. The study evaluated hepatitis B core antibody (anti-HBc), surface antigen (HBsAg) and e-antigen (HBeAg) in 330 mother-infant pairs using commercial ELISA kits (Hepanostika, Organon Teknika). All tests, calculation of cut-off and elimination of outlying control values were performed according to manufacturer's instructions. Data was analysed using STATA 5.

RESULTS

Out of the 330 maternal samples tested, 107 (32.4%) were positive for HBcAb, 18 (5.4%) for HBsAg, and 4 (1.2%) for HBeAg. The prevalence of maternal core antibody and hepatitis B surface antigenemia are shown by age group in Table 1. Hepatitis B surface antigenemia increased with maternal age.

Of the 334 samples tested for infants, 35 (10.5%) were positive for HBcAb, 1 (0.3%) for HBsAg, and all were negative for HbeAg. Table 2 shows decay of the infant's core antibody status with age by

Table 1
Maternal hepatitis B status by age group.

Maternal age (years)	Hepatitis B negative	Anti-HBc + (%)	Anti-HBc+ and HBsAg+ (% of anti-HBc +)
15-19	15	12 (44)	1 (8)
20-24	75	22 (23)	3 (14)
25-29	80	37 (32)	6 (16)
30-34	38	22 (37)	5 (23)
35 or greater	15	14 (48)	3 (21)
All ages	213	107 (32)	18 (17)

Table 2
Infant hepatitis B status by maternal core antibody status and age.

Infant age (months)	Mother anti-HBc+ Children anti-HBc+/total (%)	Mother anti-HBc- Children anti-HBc+/total (%)
0	7/7 (100)	0/26
2	11/16 (69)	0/26
3	6/16 (38)	0/25
4	2/12 (17)	0/33
5	3/15 (20)	0/27
6	1/13 (8)	0/30
7	1/10 (10)	1/33 (3)
8	3/18* (17)	0/23
All ages	34/107 (32)	1/223 (0.4)

* indicates one child also HBsAg positive

maternal anti-HBc status. Only one of the 35 core antibody positive infants had a core antibody negative mother. This was a 7 month old girl who was surface antigen negative. All 14 children of surface antigen carrier mothers who were HBeAg negative were themselves negative for HBsAg (ages ranging from 0 to 8 months old). One out of four (25%) of the children of HBeAg positive mothers was HBsAg positive, an 8 month old boy. Two of the remaining three, one 8 months old and one 6 months old were uninfected (anti-HBc negative) and one 8 month old was positive for core antibody but negative for surface antigen.

DISCUSSION

This is a relatively small cross sectional survey. The assumption is made that surface antigen positivity in adult women is due to carriage of the virus since acute infection will be rare in a prevalence survey (less than 0.5%). Nevertheless a prevalence of surface antigenemia in adult women of 5.4% confirms that hepatitis B is of intermediate prevalence in rural Bangladesh. This prevalence of carriage is normally associated with both perinatal and horizontal infection. The low proportion of women of child bearing age who are e antigen positive (1.2%) indicates that perinatal infection plays a small role in determining carriage and that child to child transmission is likely to be the major determinant of carriage. These results are similar to those reported for neighboring India -pregnant HBsAg positive women range between 1 and 6% of the population (Desai *et al*, 1993).

Infection in infants is difficult to define because of the presence of passively transferred maternal antibody. This can partially be overcome by stratification on maternal core antibody status. Table 2 clearly shows that infection is unusual amongst children of core antibody negative mothers - only one child became infected up to the age of 8 months. The core antibody positivity prevalence in infants of core antibody positive mothers declines up to the age of six months, with some increase in 7 and 8 month old infants. This pattern suggests that infection may be occurring at these older ages.

Infection in adult women shows an increasing prevalence with age and there is some suggestion of higher rates of infection in the youngest age group. This increase with age is presumably due to increasing sexual exposure. The increased rate in the youngest age group is not statistically significant but may indicate a rising incidence of infection amongst young women. The relatively small proportion of these infections which are associated with carriage (8%) suggests that the infections are occurring in adolescence.

The prevalence of carriage in this population clearly justifies introduction of universal hepatitis B vaccination for prevention. The relative unimportance of perinatal infection indicates that this can be carried out as part of the routine Expanded Program on Immunization at ages, 2, 3 and 4 months without the need for a dose given immediately after birth. This strategy, however, is a long term goal. Since rates of hepatitis B infection (and presumably acute hepatitis) rise in adolescence and adult life, there is an additional need at present for preventive strategies at these ages through blood product screening and control of sexually transmitted infections.

ACKNOWLEDGEMENTS

This research was supported by the ICDDR, B: Center for Health and Population Research and Ford Foundation. The Center is supported by over 30 different countries and agencies which share its concern for the health and problems of developing countries.

REFERENCES

de Francisco A, Hall AJ, Unicomb L, Chakraborty J, Yunus Md, Sack RB. Maternal measles antibody decay in rural Bangladeshi infants- implications for vaccination schedules. *Vaccine* 1998; 6: 564-8.

Desai HG. Viral hepatitis and pregnancy. *J Assoc Physicians India* 1993; (suppl 2): 4-5.

Edmunds WJ, Medley GF, Nokes DJ, Hall AJ, Whittle HC. The influence of age on the development of the hepatitis B carrier state. *Proc R Soc Lond B* 1993;253: 197-201.

Hall AJ. Control of hepatitis B by childhood vaccination. *Rev Med Microbiol* 1994; 5: 123-30.

Islam MN. Viral Hepatilis-past and present. Hepatitis-B virus infection in Dhaka, *Bangladesh Med Res Counc Bull* 1984; 13: 16-26.

Mustafa, M, Islam MN, Rahman M, Sattar H. Prevalence of hepatitis B surface antigen (HBsAg) among prostitutes at Dhaka. *Bangladesh Med Res Counc Bull* 1986; 15: 67-71.

Sattar H, Islam MN. Hepatitis B virus markers among the prostitutes of Dhaka. *Bangladesh Med Res Counc Bull* 1996; 22: 8-11.

Zaman S, Khan M, Alam K, Williams R. Primary hepatocellular carcinoma and viral hepatitis B and C infection in Bangladeshi subjects. *J Trop Med Hyg* 1995; 98: 64-8.