

## EPIDEMIOLOGY OF PERSISTENT HEPATITIS B VIRUS INFECTION

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### INTRODUCTION

The prevention of spread of Hepatitis B Virus (HBV) in hospitals as well as in the general population is of great importance since HBV infection can result in much human disability. HBV associated chronic liver disease and the association between HBV infection and liver cancer has made hepatitis B a very significant public health problem.

### PREVALENCE OF HEPATITIS B SURFACE ANTIGEN AMONG BLOOD DONORS

To ensure safe blood transfusion, screening of blood donors for the Hepatitis B surface antigen (HBsAg) at the National Blood Services Centre (NBSC) was started in 1972, using the immunoelectroosmophoresis (IEOP) method. Preliminary screening of 9932 blood donors revealed an overall prevalence of 1.4%<sup>1</sup> (Table 1) There appeared to be a higher prevalence in the Chinese (2.2%) when compared to Malays (1.6%) and Indians (0.4%). A very high prevalence was noted in East Malaysians (11.4%). The prevalence rate of HBsAg among Malaysians was about 17 times higher than the rates observed in blood donors in the United Kingdom and the United States, where the carrier rate using the IEOP method is less than 0.1%.

The more sensitive radioimmunoassay (RIA) method for screening HBsAg was introduced at the NBSC in 1979. This technique is now the standard method used in most good transfusion centres around the world. In 1984 a large population of donors (24,747) was screened for HBsAg (Table 2). In this series an overall prevalence of 3.14% was found. The prevalence rate in the Malays was 2.9%, in the Chinese 5.02% and in the Indians 0.8%. This relatively low positive rate among the Indians has been a consistent finding in several seroepidemiological studies.

A survey of HBsAg positive blood donors showed that HBeAg was present in about 50% of cases<sup>2</sup> (Table 3). These figures suggest therefore that as many as between 400 – 500 of our 26,000 donors or so annually, may develop chronic hepatitis and thus be at risk to developing long term sequelae like cirrhosis and primary hepatocellular carcinoma (PHC). Ten to 15% of HBsAg positive donors show evidence of transient subclinical infection.

### PREVALENCE OF INFECTION IN HOSPITAL SETTINGS

Screening of patients and staff in the haemodialysis unit at the Kuala Lumpur General Hospital has been a routine procedure over the years. In 1978 a study was undertaken to determine the risk of infection in the unit. Findings indicate a high exposure rate in both patients and staff, with HBsAg carriage in patients and staff as high as 40% and 12% respectively.<sup>3</sup> In a separate study conducted in 1985 it was found that 15% of the staff of the haemodialysis unit were positive for HBsAg while no carriers were found among the staff of the urology and the cardiothoracic units.<sup>4</sup> The exposure rate has also been noted to be particularly high among anaesthetists.<sup>5</sup>

The response to active immunisation with HBV vaccine among staff and patients of the haemodialysis unit was studied. It was found that 100% (17/17) of the laboratory staff, 92.9% (13/14) of the haemodialysis unit staff and 80.8% (21/26) of patients developed antibodies to HBsAg after the third injection of vaccine. In none of the recipients of the vaccine, was HBsAg detected in the blood at any time. It was concluded that there was a good response to Hepatitis B vaccination in both staff and patients of the haemodialysis unit.<sup>6</sup>

Among clinically diagnosed cases of viral hepatitis admitted to the Kuala Lumpur General Hospital, at least 33% were due to Hepatitis A virus. 14% were due to hepatitis B virus while 50% may be due to non-A non-B virus infection.

### PREVALENCE IN ANTE-NATAL MOTHERS

To date, a total of 6899 pregnant women in two areas of Kuala Lumpur has been screened for HBsAg (Table 4). Included in this survey were 4674 Malays, 966 Indonesians, 660 Chinese and 567 Indians. 10.1% of Indonesian mothers, 5.6% of Chinese, 2.2% of Malays and 0.8% of Indians were HBsAg reactive. 41.5% of all mothers who were positive for HBsAg were also positive for HBeAg. The breakdown of the HBeAg positive mothers into the various ethnic groups, as well as the figures for those positive for anti-HBeAg are summarised in Table 5. Ninety

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TABLE 1

SCREENING FOR HEPATITIS B SURFACE ANTIGEN IN BLOOD DONORS BY  
THE IEOP METHOD (1972).

Race	No. Screened	No. Positive	% Positive
Malay	5,688	90	1.6
Indians	2,129	8	0.4
Chinese	1,520	33	2.2
East Malaysians (natives)	88	10	11.4
Others	507	5	1.0
Total	9,932	146	1.4

TABLE 2

PREVALENCE OF HBsAg IN BLOOD DONORS (1984)

Race	No. tested	No. of HBsAg +	(%)
Malay	11,069	318	(2.90%)
Chinese	8,071	405	(5.02%)
Indian	5,022	40	(0.80%)
Others	495	14	(2.82%)

TABLE 3

HBeAg AND anti-HBe IN 325 HBsAg POSITIVE BLOOD DONORS (1984 – 1985)

Race	No. investigated	HBeAg +	Anti-HBe +	HBeAg <sup>-</sup> and Anti-HBe +
Malay	122	66 (54.1%)	51 (41.8%)	5(4.1%)
Chinese	183	99 (54.1%)	78 (42.6%)	6 (3.3%)
Indian	15	5 (33.3%)	8 (53.3%)	2(13.3%)
Others	5	3 (60.0%)	2 (40.0%)	0
Total	325	173 (53.2%)	139 (42.7%)	13 (4%)

eight babies who were born to HBsAg positive mothers are now under study. Four (4.1%) of 98 babies were found to be HBsAg positive at birth and all 4 of these babies were born to mothers who were both HBsAg and HBeAg positive. These 4 cases have remained persistently positive. In these cases, infection had probably occurred in utero. Another six babies born of e antigen positive mothers showed evidence of persistent infection and the development of a chronic carrier state. These represented the group of babies who were not available for early vaccination and whose initial HBsAg status were not known. Three babies born of mothers who were HBsAg positive but HBeAg negative, showed transient HBsAg carriage. This indicates that though babies of HBeAg negative mothers are at a lesser risk of becoming chronic HBsAg carriers, vaccination is still desirable. Eighty one other babies who received vaccination has so far, from regular follow-up, showed no evidence of HBV infection, thus indicating a high efficacy of vaccination in infants at risk.

**PREVALENCE OF HBsAg AMONG HAEMOPHILIACS**

Investigation of 90 haemophilic patients revealed a HBsAg carriage rate of 6.9%. Eighty three percent had anti-HBsAg and anti-HBc, indicating a high rate of exposure to HBV infection. A high proportion of these patients had evidence of liver dysfunction. This could possibly be due to non A, non B virus infection.

**MANAGEMENT**

Blood donors who are HBsAg positive are regularly followed up as newer therapeutic regimens may one day benefit the more

severely affected. So far interferon has been used in four patients with chronic hepatitis. Two patients, a Chinese and a Caucasian, developed anti-HBe and became HBeAg negative. There were no changes in the two other patients. Interpretation of these results is difficult at the present.

**DISCUSSION**

Studies in Malaysia so far have shown a high prevalence rate of HB infection with carrier rates ranging from 3 to 11% depending on the ethnic group. There is also a high exposure rate (up to 50%) to HBV in the population as well as a significant incidence of acute and chronic hepatitis. The prevalence of HBV infection was found to be significantly higher in the haemodialysis unit of KLGH. An antenatal screening programme has been undertaken to determine the frequency of both vertical and perinatal transmission of HBV among the various ethnic groups. Data from this will help in establishing the feasibility of a vaccination programme in high risk infants.

The availability of markers other than HBsAg has provided additional information with regards to prognosis. Screening of potential vaccinees for these markers could indicate that vaccination may not be necessary, hence resulting in saving of costs.

As there is a strong association of HBV infection with PHC, a marker to detect the progression of HBV positive liver cirrhosis to PHC is therefore of vital importance. In a collaborative study to establish such a marker, 5-nucleotide phosphodiesterase isoenzyme V was found to be useful in the detection of PHC.<sup>8</sup> Monitoring of the marker in relevant cases is advised. Other collaborative studies

TABLE 4

ANTENATAL SCREENING FOR HBsAg

Race	No. investigated	HBsAg +	%
Malay	4674	104	2.2
Chinese	660	37	5.6
Indian	567	5	0.8
Indonesian	955	96	10.1
Others	43	0	
	6899	242	3.5

TABLE 5

HBeAg, Anti-HBe IN HBsAg+ MOTHERS ACCORDING TO RACE

Race	No. investigated	HBeAg+	Anti-HBe +	HBeAg-/ anti-HBe -
Malay	102	31 (30.4)*	61 (59.8)	10 ( 9.8)
Chinese	33	19 (57.6)	10 (30.3)	4 (12.1)
Indian	3	1 (33.3)	1 (33.3)	1 (33.3)
Indonesian	67	37 (55.2)	23 (34.3)	7 (10.5)
Total	212	88 (41.5)	95 (44.8)	22 (10.4)

\*One positive for both HBeAg and anti-HBe  
 Figures in paratheses are percentages

employing DNA technology, showed the importance of HBV infection in immunodeficiency syndromes. The study of HBV in leucocytes has revealed some new aspects regarding the epidemiology of HBV infection. Since HBV is a double stranded DNA virus, it is quite possible that the presence of HBV in leucocytes may undermine the body's immunological defences.<sup>9,10</sup> In a recent study, at least 16.3% of PHC patients were found to have the virus genome in their sera." In view of the serious sequelae of HBV infection, blood donors and patients who have chronic HBV infection should be regularly followed up and monitored for the presence of HBeAg and anti-HBe. Hopefully some of these patients may one day benefit from new treatment regimens. Therapeutic trials such as combining adenosine arabinoside and interferon are currently being undertaken in some research centres.

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