ORIGINAL ARTICLE

Prevalence and Risk Factors of Hepatitis B in First-time Blood Donors at National Blood Centre after Implementation of National Vaccination Programme

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ABSTRACT

Introduction: Hepatitis B virus (HBV) infection is one of the major public health problems in Malaysia. It remains the most common permanent deferral among blood donors. In Malaysia, the national vaccination programme has been introduced since 1989 to prevent HBV transmission. The objective of this study is to determine the prevalence and associated risk factors of HBV infection among first-time blood donors after the implementation of the national hepatitis B vaccination programme. **Methods:** This is a retrospective cohort study involving tracing of the database of National Blood Centre Malaysia. The record of first-time blood donors who had donated between 1st January 2010 and 31st December 2015 and were screened HBV positive was reviewed and analysed. **Results:** There were 376,737 first-time donors who had donated blood and 575 of them screened positive for HBV. The overall prevalence of seropositive for hepatitis B was 0.15%. The prevalence was higher at 0.23% among donors born before the year 1989 (pre-vaccination era) compared to 0.05% among donors born in and after the year 1989 (post-vaccination era). Perinatal transmission was found to have 15 times higher odds of developing HBV infection as compared to those who had the combination of risk factors among those born after the year 1989 (adjusted OR=14.95, 95% CI 1.80=124.01). **Conclusion:** The implementation of the national vaccination programme reduced the prevalence of hepatitis B among donors who received vaccination at birth compared to those who did not.

Keywords: Hepatitis B virus, Blood donors, Vaccination, Seroprevalence, Risk factors

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INTRODUCTION

Hepatitis B is a vaccine-preventable infection caused by hepatitis B virus (HBV) of the hepadnaviridae family which was discovered in the 1960's by Dr. Baruch Blumberg. The surface marker of HBV was first named as Australia Antigen (AuAg) as it was discovered mainly among Australian aborigines (1). Nowadays, AuAg is referred to hepatitis B surface antigen (HBsAg). In blood transfusion service, screening for HBsAg in blood donor was first introduced in 1971. However, the initial screening tests to detect HBsAg used were immunodiffusion and counter electrophoresis, of which methods were less sensitive and ineffective to low HBsAg titre and thus, in reducing the hepatitis transfusion-transmitted infection (TTI) (2). With the advancement of technology, the risk of transfusion-transmitted HBV has steadily declined. However, HBV infection remains the most common infection detected among blood donors during screening (3).

The main routes of HBV infection include vertical transmission, which is from infected mother to child during birth or shortly after birth; and horizontal transmission, which is the exposure to infected blood or various body fluids such as saliva, menstrual, vaginal, and seminal fluids (4). Therefore, blood products from donors who are infected with HBV can be transmitted to the patient.

In Malaysia, the universal screening of hepatitis B on all blood donors has been implemented since the year 1987 (5). The serological screening was done in the earlier years and subsequently, nucleic acid testing

(NAT) was added as a part of screening tests in 2007 by the National Blood Centre (NBC) in Kuala Lumpur (6). All the donated blood is screened and if found positive, the donors will be traced and contacted for further counselling and investigations. These donors will also be deferred from future blood donation and all the donated blood products will be discarded (7).

Complications of HBV infection are severe, and these include but not limited to acute, fulminant, or chronic hepatitis, liver cirrhosis and hepatocellular carcinoma (HCC). Thus, one of the measures that has been taken to prevent the transmission of this virus is via vaccination. Vaccination has been proven effective for the prevention of HBV infection (8). In Malaysia, compulsory hepatitis B vaccination to all newborn infants was first introduced in 1989. Three doses are given with the first at birth, the second at one-month-old and the third at six-month-old (9). The reported 2016 coverage for hepatitis B vaccination in Malaysia is 99.27% (10).

Therefore, the aim of this study was to determine the prevalence of HBV infection in first-time blood donors at the NBC after implementation of the national vaccination programme. In addition, this study aimed to tabulate the donor demographic and the associated risk factors to HBV infection. Acknowledging the risk factors may help to ensure only safe donors are recruited for blood donation, which subsequently can improve the blood transfusion safety in the country.

MATERIALS AND METHODS

This is a retrospective cohort study involving medical records review of HBV screening positive blood donors. The microbiology screening for HBV in NBC involved nucleic acid testing (NAT) using Novartis Procleix (TIGRIS, USA) and HBsAg using Abbott PRISM (Germany). The inclusion criteria for this study were all first-time Malaysian blood donors that were screened positive for hepatitis B (both NAT and HBsAg) and had donated at NBC from 1st January 2010 till 31st December 2015. Regular or lapsed donors; donors who were not contactable; donors who had donated blood at another blood centre prior to donation at NBC; donors who did not turn up for investigation after notification letter were sent out; and donors who had defaulted follow-up during counselling were excluded from this study. Out of the total HBV positive first-time blood donors, 215 donors were selected via systematic random sampling.

Risk factors for HBV included in this study were high risks behaviours such as men who have sex with other men (MSM); individuals with multiple sex partners and individuals who have had sex with sex worker; perinatal transmission; parenteral transmission such as individuals who have had history of blood transfusion; tattoo; body piercing; acupuncture; surgical; and dental procedures; and individuals who co-habitate such as living with family members, a partner/partners and friends.

Ethical approval for this study was obtained from Medical Research and Ethics Committee, Ministry of Health, Malaysia and Jawatankuasa Etika Penyelidikan (Manusia), Universiti Sains Malaysia. This study was registered with the National Medical Research Register (NMRR) with research ID number 28733.

Statistical analysis was performed using IBM Statistical Package for the Social Sciences (SPSS) version 23 for windows-software (SPSS, Chicago Illinois, USA). Descriptive analysis was used to define the demographic characteristics. Simple logistic regression and multiple logistic regression were performed to test the associated risk factors for HBV infection among first-time blood donors. Factors that showed to have a significant association with HBV infection during univariable analysis were then analysed in a multivariable analysis by using multiple logistic regression. The results of the tests were expressed as odds ratios (OR) or adjusted odds ratios with 95 % confidence intervals (CI).

RESULTS

Prevalence of HBV infection

Between 1st January 2010 to 31st December 2015, a total of 807,734 donors had donated blood at NBC with 1,736 blood donors were found to be screened positive for hepatitis B. Amongst these donors, there were 376,737 first-time donors and 575 of them were screened positive for hepatitis B (Table I). A total of 215 donors were randomly selected from the pool of the first-time blood donors whom were screened positive for hepatitis B. These donors were categorised into two groups, of which for those who were born before, or born in or after the year 1989 when the hepatitis B vaccination programme was implemented nationwide. All results were shown based on the grouping, which is either pre-vaccination programme (born before 1989; <1989) or during vaccination programme (born in or after 1989; ≥ 1989).

The overall prevalence of hepatitis B among the first-time blood donors at NBC from 1st January 2010 until 31st December 2015 was 0.15%. The prevalence of hepatitis B among the first-time donors who were born in or after the year 1989 (vaccination period) was lower at 0.05% compared to the prevalence of hepatitis B among donors who were born before 1989 (pre-vaccination period) at 0.23%.

From the total of 215 study samples, 145 (67.4%) donors were born before 1989 while 70 (32.6%) donors were born in or after 1989. The age range for donors born before 1989 was between 23 to 57 years old with the mean age of 35.5 years old. For donors born in or after 1989, the age range was 17 to 26 years old with the mean age of 20.9 years old.

Table I: The distribution of donors according to the year of donation and by year of birth.

	2010	2011	2012	2013	2014	2015	Total
All donors							
< 1989	89, 953	94, 716	88, 654	90, 254	88, 833	90, 295	542, 705
≥ 1989	27, 499	37, 898	42, 322	45, 675	53, 481	58, 154	265, 029
Total	117,452	132,614	130,976	135,929	142,314	148, 449	807, 734
First-time donors							
< 1989	39, 465	39, 677	34, 263	34, 036	32, 592	33, 551	213, 584
≥ 1989	19, 743	25, 386	25, 911	26, 688	31, 867	33, 558	163, 153
Total	59, 208	65, 063	60, 174	60, 724	64,459	67, 109	376, 737
First-time donors with hepatitis B							
< 1989	68	96	67	114	83	55	483
≥ 1989	3	11	12	33	18	15	92
Total	71	107	79	147	101	70	575

Demographics characteristics and risk factors for HBV infection

The blood donors' demographics characteristics are shown in Table II. Majority of the donors were Malay and male. There were two donors, who were born after 1989 and did not receive the hepatitis B vaccination at birth.

The risk factors associated with HBV infection is shown in Table III. There were two donors who were born in or after 1989 (≥ 1989) but did not receive the vaccination at birth; thus, they were excluded in the analysis. Blood donors who had two risk factors were grouped as dual risks. This study showed that those with perinatal transmission as the risk factor had 15 times higher odds of developing HBV positive as compared to those who had a combination of risk factors among those who were born in or after 1989 (adjusted OR = 14.95, 95% CI 1.80 = 124.01).

Table II: Blood donors' demographic characteristics (N=215)

Characteristics	Year of Birth, n (%)		Total, n (%)
	<1989 (n=145)	≥ 1989 (n=70)	
Gender			
Male	109 (71.7)	43 (28.3)	152 (70.7)
Female	36 (57.1)	27 (42.9)	63 (29.3)
Race			
Malay	93 (66.0)	48 (34.0)	141 (65.6)
Chinese	43 (71.7)	17 (28.3)	60 (27.9)
Indian	1 (100.0)	0 (0.0)	1 (0.5)
Others	8 (61.5)	5 (38.5)	13 (6.0)
Hepatitis B Vaccination			
Yes	0 (0.0)	68 (100.0)	68 (31.6)
No	145 (98.6)	2 (1.4)	147 (68.4)
Risk factors			
Yes	74 (51.0)	31 (44.3)	105 (48.8)
No	71 (49.0)	39 (55.7)	110 (51.2)
Risk factors (n=105)			
a. Single risk factors			
Perinatal	1 (0.7)	8 (25.8)	9 (8.6)
Cohabitation	18 (12.4)	7 (22.6)	25 (23.8)
Parenteral	21 (14.5)	3 (9.7)	24 (22.9)
High risk behaviour	20 (13.8)	5 (16.1)	25 (23.8)
b. Combination of risk factors			
Perinatal & cohabitation	3 (2.1)	4 (12.9)	7 (6.7)
High-risk behaviour & parenteral	8 (5.5)	0 (0.0)	8 (7.6)
Cohabitation & parenteral	1 (0.7)	0 (0.0)	1 (1.0)
Perinatal & parenteral	2 (1.4)	4 (12.9)	6 (5.7)

Table III: Risk factors associated with HBV infection (N= 213)

Risk factors	Year of Birth, n (%)		Crude OR[b] (95% CI)	Adjusted OR[c] (95% CI)
	< 1989 (n=145)	≥1989 (n=68)		
Gender				
Male	109 (75.2)	41 (60.3)	Reference	
Female	36 (24.8)	27 (39.7)	1.99 (1.08-3.69) *	
Race [a]				
Malay	93 (64.1)	48 (70.6)	1.16 (0.34-3.97)	
Chinese	43 (29.7)	16 (23.5)	0.84 (0.23-3.10)	
Others	9 (6.2)	4 (5.9)	Reference	
Risk factor characteristic (n=104)				
Perinatal	1 (1.4)	8 (25.8)	14.00 (1.47-33.23)*	14.95 (1.80-124.01)*
Cohabitation	18 (24.3)	7 (22.6)	0.58 (0.16-2.07)	0.623 (0.23-1.70)
Parenteral	21 (28.4)	3 (9.7)	0.25 (0.06-1.11)	0.267 (0.08-.953
High-risk behaviour	20 (27.0)	5 (16.1)	0.44 (0.12-1.62)	0.47 (0.16-1.34)
Dual risks	14 (18.9)	8 (25.8)	Reference	

[a] The Indian respondent was analysed together with the other races for statistical purposes, [b] Simple logistic regression was performed, [c] Multiple logistic regression was performed adjusted for gender and race, * p <0.05

DISCUSSION

NBC is the largest blood collection centre in Malaysia. The average permanent deferral due to positive microbiology screening was 579 (0.35%) cases per year for NBC and 3,094 (0.48%) cases per year for the whole of Malaysia. Among the deferrals, HBV infection was found to be the main cause of deferrals and ranges 43.3% - 58.6% of total microbial-related deferral, outweighing the deferral of HIV, syphilis, and hepatitis C virus (5, 11-15).

The prevalence of HBV infection among blood donors were reported to be between 0.19%- 7.5% in previous studies (16-18). However, among the first-time blood donors, the prevalence of HBsAg positive was between 0.3% to 0.33% which were comparable with this study (19, 20). The first-time donors were chosen as the study subjects rather than regular donors because previous studies showed that the former group of donors poses a higher risk of transfusion-transmissible infection (TTI) compared to the latter (21, 22). Between the two groups of first-time blood donors (the pre-vaccination period and during vaccination period), there was a reduction of 4.6 times risk of transmission when vaccination was implemented. This signified that hepatitis B vaccination is an effective preventive measure against the viral transmission. Furthermore, the reduction of the viral transmission could also be attributed to the progressive vaccine coverage from 93.5 % in 2000 to 99.27% in 2015 (10, 23). Similar studies done in Taiwan and Italy showed that there was a reduction of HBV infection since the national hepatitis B vaccination programme implementation (24, 25).

This study also showed that the ratio of male-to-female first-time blood donors who were positive for HBV infection was of 2.4:1. Similarly, a study by Baig reported that the overall male-to-female ratio for HBV infection within Pakistani population was approximately at 4:1, and the ratio widened to 7.1:1 for the group of 36-40 years old individuals (26). Furthermore, the risk of developing HCC due to HBV infection was higher amongst male as compared to female counterpart. This scenario was demonstrated and implied by lower production of oestradiol, of which hormonal action at this level in male population led to a greater progression of hepatic fibrosis and HCC (27, 28).

In this study, racial background of the donor is according to what was selected by the donor him or herself in the blood donor enrolment form. The majority of the donors were Malays followed by Chinese and the remaining donors were Indians and other undefined races. This racial distribution nearly matched the proportion of NBC's blood donors, in general, with most are Malays followed by Chinese, Indians and other races. A study done by Meldal and colleagues, reported a racial distribution of 60% for Malays, 30% for Chinese and 10% for Indians and other races among Malaysian blood donors with HBsAg positive. This similar study also found that 80% of Chinese donors expressed genotype B whereas Malay donors expressed a similar trending occurrence of genotype B and C (29). Meanwhile, Ng and colleagues reported that there was a higher HBV seroprevalence amongst the Chinese undergraduates followed by Malay, Indian and other ethnic minorities (30).

Malaysia is a low endemicity area of HBV infection with HBsAg prevalence is less than 2% (31). From this study, it is found that perinatal transmission was significantly associated with HBV infection. A child born to an infected mother, even if vaccination was given, will still be at risk of acquiring HBV infection due to repeated exposures. The transmission of HBV between family members may occur through frequent exposure to blood, such as contact with skin lesions; saliva through sharing of utensils and toothbrushes; or breast milk (32). A study reported that adopted children, who were HBsAg positive, were also a source of HBV infection to their foster family (33). Moreover, a study done in Brazil, also reported that a positive family history of HBV infection, sharing personal objects and history of blood transfusion were significant risk factors associated with chronic HBV infection (34). In contrast, a study done in Bahrain revealed that surgical procedures were the main sources of HBV infection (35).

Risk factors may also vary based on HBV infection endemicity. In countries where HBV endemic is high (>8% HBsAg prevalence), vertical and perinatal transmission is the main route of transmission. However, in low endemicity (<2% HBsAg prevalence), HBV is usually transmitted horizontally such as through parenteral routes and sexual contact (36). Nevertheless, the prevalence of categorisation may change with the impact of hepatitis B immunisation and other prevention programmes.

One of the measures to improve blood safety is through donor questionnaires prior to blood donation. There were donors who donated their blood despite having risk factors for HBV infection. Wong and his colleagues reported that amongst Hong Kong's blood donors, as high as 10% of the donors did not disclose their risk factors of TTI-associated lifestyle during donation (37). Similarly, in this study, most of the donors revealed their risk factors of HBV infection only upon counselling and repeated blood investigation but not during the blood donation. When inquired as to why the donors did not reveal their risk factors, the reasons include but not limited to lack of TTI-awareness and avoidance to discuss their sexual preference during blood donation. Hence, it is important to educate the blood donors about TTI-associated lifestyle and the impact towards

transfusion safety.

A further approach to reduce HBV transfusion-transmission is via implementation of more sensitive screening tests such as the introduction of HBV NAT screening test and adoption of hepatitis B core antibody (anti-HBc). NAT screening potentially detects HBV in very early acute phase, during the late chronic phase where HBsAg levels are very low and to detect HBV escape mutants. Additional testing with anti-HBc is beneficial in detecting HBV in chronic carrier state and at the end of an acute resolving infection where HBsAg may be undetectable (38). Additionally, pathogen inactivation of blood products using solvent-detergent techniques or photochemical inactivation techniques, such as THERAFLEX®, INTERCEPT®, Mirasol® and Cerus S-303 INTERCEPT® has been effective in inactivating a wide range of viruses, bacteria, and parasites (39). Thus, these technologies have further improved the blood safety.

Nevertheless, there are some limitations to this study. As the study subjects involved only first-time donors of NBC, the results may not be reflective toward the whole population of Malaysia. Furthermore, the ethnic population in this study (Malay, Chinese and Indian) is mainly reflected the general population of Peninsular Malaysia whereas, in Sabah and Sarawak, there are more indigenous ethnic groups such as Kadazan, Dusun, Iban, and Bidayuh. Besides, Sabah was also reported as a state with the highest number of donors with positive HBV infection (5). Another limitation to this study is the frequency and duration of exposure to each risk factors which were not taken into consideration. Perhaps a future study is necessary to address all these limitations.

CONCLUSIONS

This study demonstrated that the prevalence of hepatitis B among first-time blood donors at NBC decreased after the implementation of the national hepatitis B vaccination programme. Furthermore, perinatal transmission had a significant association with HBV infection. Besides microbiology blood screening, it is also important to educate future blood donors regarding risk factors associated with HBV infection as a mean to improve the safety of blood transfusion within this country.

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