

ORIGINAL ARTICLE

High Incidence of Hepatitis B Virus Infection in Hemodialysis Patients at Sanglah General Hospital and Its Risk Factors

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ABSTRACT

Background: Patients receiving maintenance hemodialysis (HD) are at higher risk for hepatitis B virus (HBV) infections than in general population. Strict infection control is essential to prevent nosocomial transmission. We aimed to investigate the incidence of HBV infection in the HD population in Sanglah General Hospital as well as risk factors acquired HBV infection.

Method: All adult patients receiving maintenance HD ($n=267$) in 3 dialysis units at Sanglah Hospital were studied between March to June 2016. In this study, medical record of patients on maintenance hemodialysis were reviewed and the patients were interviewed by the researchers to collect data regarding the serology status of these patients before and during HD, and potential risk factors which could be associated with HBV acquisition.

Results: Participant mean age was 54.07 ± 0.80 years and 154 (57.7%) were male. We found 21 patients (7.8%) were sero-positive for HBV (HBsAg positive) with mean titer was 9.26 ± 1.85 . Of the sero-positive patients, 1 patient (4.8%) were known to be infected before the initiation of HD and 20 patients (95.2%) were infected during HD. Incidence of HBV infection during HD was 7.5% (20/266). Sero-positive patients were younger with mean age was 51.81 ± 2.76 years, had longer time on dialysis and had previous blood transfusions. Risk factors, which significant associated with hepatitis B infection were history of transfusion ($p < 0.01$; OR = 2.49; 95% CI: 1.29-8.18) and duration of hemodialysis ($p < 0.01$; OR = 1.07; 95% CI: 1.03-3.74).

Conclusion: Patients on maintenance HD in Sanglah General Hospital have a high incidence of HBV infection. The factors associated with HBV infection are highly suggestive of nosocomial transmission within HD units. History of transfusion and duration of hemodialysis were significant risk factors for HBV infection in patients receiving maintenance HD.

Keywords: hemodialysis, hepatitis B, incidence, risk factor

ABSTRAK

Latar belakang: Pasien-pasien yang menerima perawatan hemodialisis (HD) berada pada risiko yang tinggi untuk terinfeksi virus hepatitis B dibandingkan populasi umum. Kontrol terhadap kejadian infeksi sangat

penting untuk mencegah penularan nosokomial. Penelitian ini bertujuan untuk menyelidiki kejadian infeksi virus hepatitis B pada populasi HD di Rumah Sakit Umum Sanglah serta faktor risiko penularan infeksi virus hepatitis B pada populasi HD.

Metode: *Semua pasien dewasa yang menerima perawatan HD rutin (n = 267) di 3 unit dialisis di Rumah Sakit Sanglah dipelajari antara Maret-Juni 2016. Dalam penelitian ini, rekam medis pasien pada perawatan hemodialisis ditinjau dan pasien diwawancarai oleh peneliti untuk mengumpulkan data mengenai status serologi pasien sebelum dan selama HD, dan faktor-faktor risiko potensial yang dapat dikaitkan dengan penularan virus hepatitis B.*

Hasil: *Usia rata-rata pasien adalah $54,07 \pm 0,80$ tahun dengan 154 (57,7%) orang laki-laki. Kami memperoleh 21 pasien (7,8%) yang sero-positif untuk virus hepatitis B (HBsAg positif) dengan titer rata-rata adalah $9,26 \pm 1,85$. Dari pasien yang sero-positif, 1 pasien (4,8%) diketahui terinfeksi sebelum memulai HD dan 20 pasien (95,2%) terinfeksi pada saat HD. Angka kejadian infeksi virus hepatitis B selama HD adalah 7,5% (20/266). pasien sero-positif yang lebih muda dengan rata-rata usia adalah $51,81 \pm 2,76$ tahun, memiliki durasi yang lebih lama untuk hemodialisis dan memiliki riwayat transfusi darah sebelumnya. Faktor risiko yang signifikan yang terkait dengan infeksi virus hepatitis B adalah riwayat transfusi ($p < 0,01$; OR = 2,49; 95% CI: 1,29-8,18) dan durasi hemodialisis ($p < 0,01$; OR = 1,07; 95% CI: 1,03-3,74).*

Simpulan: *Pasien yang menjalani HD rutin di Rumah Sakit Umum Sanglah memiliki insiden tinggi infeksi virus hepatitis B. Faktor yang terkait dengan infeksi virus hepatitis B sangat dicurigai melalui penularan nosokomial dalam unit HD. Sejarah transfusi dan durasi hemodialisis merupakan faktor risiko yang signifikan untuk infeksi virus hepatitis B pada pasien yang menerima perawatan HD.*

Kata kunci: *hemodialisis, hepatitis B, angka kejadian, faktor risiko*

INTRODUCTION

Chronic hemodialysis patients are at high risk for infection because the process of hemodialysis requires vascular access for prolonged periods. Patients receiving maintenance haemodialysis (HD) therapy are at increased risk for acquiring these infections and have a higher prevalence of hepatitis B virus (HBV) infection than in general population.^{1,2} In an environment where multiple patients receive dialysis concurrently, repeated opportunities exist for person-to-person transmission of infectious agents, directly or indirectly via contaminated devices, equipment and supplies, environmental surfaces, or hands of personnel. Furthermore, hemodialysis patients are immunosuppressed.²

Prior to effective screening of blood donations, HBV infection was associated with blood transfusions needed to correct the anaemia associated with kidney disease but patient to patient transmission in HD units is also reported.^{3,4,5,6} HBV infection is usually due to patient to patient transmission within HD units.⁷ Recognition of the risk of nosocomial infection has resulted in recommendations that strict infection control procedures should be in HD units; patients with blood-borne virus infections should be isolated from sero-negative patients during dialysis and patients as well as staff should be vaccinated against hepatitis B.^{8,9} The introduction

of blood donor screening and a reduction in blood transfusions due to the availability of recombinant erythropoietin has significantly reduced the incidence of new HBV infections among HD patients in many countries.^{10,11,12} The prevalence of HBV infection in HD patients in Indonesia is still unclear. Several studies have been conducted in West Java found 6.8% HD patients had HbsAg seropositive.¹³ While research in Yogyakarta found 11.2% HD patients had HbsAg seropositive.¹⁴ Some HD centre are not reported the prevalence of HBV infection in their centre.

Indonesia provides free access to maintenance HD for end stage kidney disease through a rapidly expanding network of centres. The national dialysis practice guidelines or infection control policies enforced by health care authorities is general agreement that patients on HD should be screened for HBV and hepatitis C virus (HCV) infection before the initiation of HD and monitored every 3–6 months thereafter.¹⁵ Sero-positive patients are dialysed on dedicated machines either in an isolated area or alongside sero-negative patients if space does not allow isolation.¹⁶ Although the prevalence of HBV in patients with end stage renal failure (ESRF) undergoing dialysis has decreased significantly during the past few decades, it is still a distinct clinical problem, as the immunosuppressive nature of renal disease often

leads to chronicity of the viral infection and results in an opportunity for nosocomial spread of the infection among dialysis patients.^{1,17} Hepatitis B research on HD patients in Bali has not been reported, therefore, researchers are interested to know the incidence of HBV infection in HD patients in Bali. This study aimed to investigate for the first time the incidence of HBV infection in the entire HD population of Denpasar.

METHOD

This descriptive study was carried out in 3 dialysis units at Sanglah General Hospital to investigate the incidence of HBV infection in HD patients (n = 267) from March 2016 to June 2016. The data was collected regarding all adult patients in maintenance HD facilities. Large and medium capacity HD facilities were visited by the researchers in order to collect data. Patient medical records were used to obtain patients age, gender, time on HD, medical history, seropositivity to HBV as well as other laboratory results. These included history of blood transfusions and history of surgery. Sero-positivity to HBV was defined by detection of hepatitis B surface antigen (HBsAg) by enzyme linked immunoassay (ELISA). ELISA tests were performed in local laboratories. Data of HBsAg patient in the beginning of HD were collected too, to know the base line status of HBV infection.

Data are presented as mean \pm SD if normally distributed or median (interquartile range) if not. Analysis was performed using SPSS version 16.0.

A Chi-square test was used to compare frequencies between groups. A t-test was used to compare means between groups for data with normal distribution or Mann–Whitney test for non-parametric data.

RESULTS

Participant mean age was 54.07 ± 0.80 years with median age of adult HD patients included was 54 years (range 20–86 years) and 57.7% were male. A total of 21 patients (7.8%) were sero-positive for HBV (HBsAg positive). Patients were grouped based on HBV infection status. Group patient with HBV infection was comprised of 21 (7.8%) patients who were HBsAg positive. Group without HBV infection consisted of 246 (92.2%) patients who were HBsAg negative. Sero-positive patients were younger with mean age was 51.81 ± 2.76 years, had longer time on dialysis (5.21 ± 1.20 years) and had previous blood transfusions. The baseline demographic and laboratory data characteristics of the patients are summarized in Table 1.

In the beginning of HD, from the medical record, we know that 1 patient (4.8%) was to be infected before the initiation of HD and 20 patients (95.2%) were infected during HD. Incidence of HBV infection during HD was 7.5% (20/266). Analysis of possible risk factors for HBV infections is shown in Table 2. Only duration of dialysis ($p < 0.01$; OR: 1.07; 95% CI: 1.03-3.74) and history of previous transfusion ($p < 0.01$; OR: 2.49; 95%CI: 1.29-8.18) were significantly different between patients who sero-converted and those who remained sero-negative.

Table 1. Demographic and laboratory data characteristics of the patients

Variable	Total Patient (n = 267) n (%)	Patient with hepatitis B (n = 21) n (%)	Patient without hepatitis B (n = 246) n (%)	p value
Age (year)	$54.07 \pm 0.80^*$	$51.81 \pm 2.76^*$	$54.01 \pm 13.2^*$	0.3
Gender				0.4
Male	154 (57.7)	13 (61.9)	141 (58.5)	
Female	113 (42.3)	8 (38.1)	105 (41.4)	
Age category (year old)				0.19
< 60	183 (68.5)	17 (80.9)	166 (67.4)	
≥ 60	84 (31.5)	4 (19.1)	80 (32.6)	
Duration of HD (year)	$4.87 \pm 0.80^*$	$5.21 \pm 1.20^*$	$4.56 \pm 7.21^*$	0.03
Duration of HD (years)				< 0.01
≤ 2	100 (37.5)	3 (14.2)	97 (39.4)	
> 2	167 (62.5)	18 (85.8)	149 (60.6)	
History of transfusion				< 0.01
Yes	156 (58.4)	20 (95.2)	136 (55.2)	
No	111 (41.6)	1 (4.8)	110 (44.8)	
History of Surgery				0.4
Yes	249 (93.2)	20 (95.2)	229 (93.1)	
No	18 (6.8)	1 (4.8)	17 (6.9)	
ALT (U/L)	$22.15 \pm 1.50^*$	$30.12 \pm 2.38^*$	$17.81 \pm 0.76^*$	0.09
AST (U/L)	$21.95 \pm 1.08^*$	$24.52 \pm 6.83^*$	$19.77 \pm 5.51^*$	0.1
Albumin (g/dL)	$4.10 \pm 0.39^*$	$3.99 \pm 0.38^*$	$4.16 \pm 0.39^*$	0.4

*SD, mean; HD: hemodialysis; ALT: alanine aminotransferase; AST: aspartate aminotransferase

Table 2. Analysis of risk factors of hepatitis B infection on HD population

Variable	Patient with hepatitis B (n = 20) n (%)	Patient without hepatitis B (n = 246) n (%)	OR	95% CI	p value
Age category (year old)					
< 60	16 (80)	166 (67.4)	2.06	0.67-6.32	0.19
≥ 60	4 (20)	80 (32.6)			
Duration of HD (years)					
≤ 2	2 (10)	97 (39.4)	1.07	1.03-3.74	< 0.01*
> 2	18 (90)	149 (60.6)			
History of transfusion					
Yes	19 (95)	136 (55.2)	2.49	1.29-8.18	< 0.01*
No	1 (5)	110 (44.8)			
History of surgery					
Yes	19 (95)	229 (93.1)	1.49	0.18-11.79	0.703
No	1 (5)	17 (6.9)			

*p < 0,05; HD: hemodialysis

DISCUSSION

Patients on maintenance HD are among the group at highest risk for HBV infection. Most HBV infection outbreaks in patients in HD units are caused by cross-contamination via the following factors: (1) Environmental surfaces, supplies (*e.g.*, hemostats and clamps), or equipment that is not routinely disinfected after each use; (2) Multiple dose medication vials and intravenous solutions that are not used exclusively for one patient; (3) Medications for injection that are prepared in areas adjacent to areas where blood samples are handled; and (4) Staff members who simultaneously care for both HBV-infected and susceptible patients. The risk of HBV transmission from blood contaminated items in this setting is greater and more serious than would be expected for other common blood borne viruses.^{1,2,4}

In general the observed incidence of HBV infection (7.5%) is higher to the general population and higher than reported in HD patients in other regions including Europe (4.1%), Japan (2.2%) and the USA (2.4%).¹⁸ A study sample from the dialysis outcome and practice patterns study that included 8615 adult HD patients from 308 dialysis facilities in Western Europe and the United States, reported incidence rates for HBV infection ranging from 0-6.6%.¹⁹ Studies from less developed countries estimated that the proportion of HBsAg carriers in the HD population varies from 2% to 20%.²⁰⁻²³ A recent multicenter prospective cohort study among dialysis patients in Korea revealed that 7.1% were HBsAg-positive.²¹ In Vietnam, 7% of HD patients tested positive for HBsAg.²² Several studies have also been performed in Indonesia, studies were conduct in West Java and Yogyakarta, they report that the prevalence of HBV infection in HD patient were 6.8% and 11.2%.^{13,14}

Some countries have different policies regarding blood transfusions and the use of special machines HD in patients with HBV infection are becoming some factors that influence in the transmission of HBV. In some developed countries, precautions HBV infection during blood donation and when initiation of HD might have been better than the developing countries. Giving the vaccine has also been routinely performed on patients undergoing HD regular. While in Indonesia, especially in Bali, is not routinely performed.¹⁵⁻¹⁷

The prevalence and incidence of HBV infections in HD patients reflects the prevalence of these infections in the general population, the quality of healthcare services in a community and the standards of infection control practices in HD units. The importance of HBV as a health risk in patients on HD is illustrated by observation that 3% of deaths in Libyan HD patients during a 1 year observation period were due to liver failure and that 13 of the 14 patients who died of liver failure were sero-positive for HBV.²⁴

Our data show that sero-positive patients were younger on average than sero-negative patients. This observation is in agreement with a previous report from Libya showing that the highest prevalence of HBV infection was observed in HD patients aged 36–55 years.^{25,26} Other studies have reported a higher prevalence of HBV sero-positivity in older patients and the reason for this difference is not clear.¹⁶ On the other hand, the prevalence and incidence of HBV sero-positivity was significantly related to the length of time on HD. This is consistent with nosocomial transmission related to dialysis since longer duration of dialysis represents a longer period at risk of acquiring an infection. Similar observations have been reported by other authors.^{27,28} Prevention of nosocomial transmission is importance in HBV infection transmission.

A positive history of blood transfusions was strongly associated with HBV infection. Prior to the introduction of effective screening of blood donors, blood transfusions were recognized as the leading source of HBV infection and some of these infections may have been acquired before adequate screening was introduced.^{29,30} In addition it is possible that some blood donors with HBV infection are being missed by current screening procedures and these may need to be reassessed.^{31,32} A large proportion of patients had previously received blood transfusions. The risk of infection could therefore be further reduced by more effective management of anemia with iron supplementation and erythropoietin.³³

Another concern raised by the current study is that HBV infection was associated with duration of HD. The positive association between HBV prevalence and years on hemodialysis has been found previously. Albertoni et al reported a sharp increase in HbsAg carriers in patients with 10 years or more of hemodialysis, a finding they attributed to a cohort effect.³⁴ In our study demonstrate a markedly higher HBV prevalence in patients with 3 years or more of hemodialysis (Figure 1). The positive association between HBV prevalence and years of hemodialysis has several possible explanations. Although less likely, it is possible that patients who have undergone hemodialysis for a longer period of time have a longer time at risk for exposure to HBV than those patients who have been on hemodialysis for a shorter amount of time.

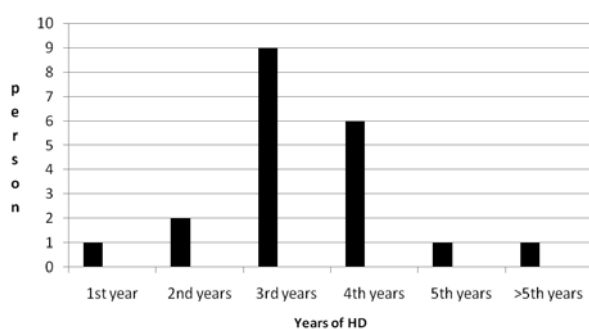


Figure 1. Variation in hepatitis B virus (HBV) prevalence by patient's time on dialysis

In general hospitals in Indonesia, dialyzers are commonly reused up to a maximum of eight times for all patients. Following the recommendations for HBV and HCV infection control issued by the Indonesian Society of Nephrology, separate rooms are available for patients who are HBsAg seropositive. Based on the slightly higher prevalence of HBV infection among HD patients than the general population (2.5-10%)

in Indonesia, there is a strong possibility that the prevalence of HBV infections among HD patients is caused by nosocomial infections.^{23,24} Our study also showed that the HD duration and number of blood transfusions were significantly associated with HBV infection.

A striking observation from this study is the wide variation in incidence and prevalence of HBV infections among different HD units. Most facilities faced a problem of increasing number of patients and most of them responded by adding more HD stations at expense of space and staff. Infection control precautions also varied widely between centres. They were strictly enforced in some places but frequently breached in others. This seemed to depend on staff initiative rather than national guidelines. On the other hand, dialyser reuse was not permitted and all bloodlines as well as other consumables were disposed after a single use.¹³ Some brands of HD machines were equipped with a sphygmomanometer. Otherwise, most non-disposable instruments used in HD environment were shared between sero-positive and sero-negative patients. The use of multi-dose vials of heparin was common and is likely to have been an important cause of nosocomial infections. Many patients started HD without being vaccinated against HBV. Even in vaccinated patients the antibody titre was not assessed. The wide variation in HBV prevalence and incidence between dialysis centres implies that there is potential to reduce blood-borne virus infection by transferring best practice from HD centers with low infection rates. In particular infection control procedures should be investigated in centers with high infection rates and the use of multidose heparin vials must be stopped urgently. Previous studies from the region show that with appropriate intervention HBV infection rates in HD centers may be substantially improved. For example in Iran, HBV prevalence reduced from 14.4% in 1999 to 4.5% in 2006 and in Saudi Arabia from 2.4% in 2001 to 0.2% in 2005.^{35,36}

Several limitations of this study should be conceded. Medical records were often incomplete and additional clinical information was frequently obtained by interviewing staff and patients. Data regarding hepatitis B core antibodies (HBcAb) or hepatitis B DNA were not available. In one recent study of haemodialysis patients in Egypt who were negative for HBsAg, hepatitis B DNA was detected in 4.1% and HBcAb in 20%.³⁷ It is therefore possible that we failed to detect cases of occult hepatitis B infection.

CONCLUSION

In conclusion, patients on maintenance HD in Sanglah Hospital Denpasar have high incidence rates of HBV infection. The factors associated with HBV infection are highly suggestive of nosocomial transmission within HD units. In our study, history of transfusion and duration of hemodialysis were significant risk factors for HBV infection in patients receiving maintenance HD. Urgent action is required to improve infection control measures in HD centers and to reduce dependence on blood transfusions for the treatment of anemia.

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