

# Serology for Hepatitis B Virus Inhemodialysis Patients: What is Necessary?

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## Abstract

**Aim:** This was a quality improvement study to evaluate immune status for Hepatitis B virus (HBV) in patients on Hemodialysis (HD) and to improve vaccination rates in these patients.

**Methods:** A prospective quality control study aimed at assuring adequate immunity for HBV in HD patients. Fifty-nine patients on HD were included during two-month study period. The inclusion criteria are all in patients with renal failure requiring HD. The following serologies were checked: HBs Ag, HBs Ab titer, and HBc Ab total. Serum samples were tested using Enzyme linked immunosorbent assay (ELISA) methods. Vaccination was offered to all patients with no evidence of protective Hepatitis B antibody (HBsAb titer) that is titer<10.

**Results:** Out of 59 patients selected in the study, 48 had prior or current vaccination. Among the vaccinated patients, only 29 patients (60.4%) had HBs Ab titers in protective range (titers>10). We also found 6 patients with Hepatitis C virus antibody (HCV Ab) positive.

**Conclusion:** HBV is the leading cause of blood-borne transmission particularly in inpatient HD units. Monitoring HBV serology (HBs Ag, HBs Ab, HBc Ab) on a routine basis is essential to prevent HBV outbreaks within HD units. Monitoring HBs Ag alone is insufficient and should be coupled with additional serology to ensure adequate protection for this particularly vulnerable population. Initiation of early vaccination in patients with DM, chronic kidney disease (CKD), especially in inpatient facilities will ensure better protection.

**Keywords:** Hemodialysis; Hepatitis B; Vaccination

**Abbreviation:** Hbsag: Hepatitis B Surface Antigen; Hbsab: Hepatitis B Surface Antibody; HB C Ab: Hepatitis B Core Antibody; HD: Hemodialysis; CKD: Chronic Kidney Disease

## Introduction

HBV is a DNA virus that is capable of causing significant liver diseases including acute hepatitis, chronic hepatitis, and cirrhosis and hepatocellular carcinoma. According to the Centers for Disease Control and Prevention (CDC) report, the estimated total number of new cases of HBV infection dropped from 225, 000 cases in 1998 to 38,000 cases in 2009 [1]. It is estimated that the total number of persons living with chronic HBV infection is between 800,000 and 1.4 million while the percentage of persons to have ever been infected with HBV is 4.3-5.6% of the total US population [2]. HBV vaccination has been available in the US since 1982. The current DNA recombinant vaccine was licensed in 1990 [3].

HBV is an efficiently transmitted blood borne pathogen. The reported transmission rate of HBV via needle exposure with contaminated blood from HBe Ag positive source is up to 30% [4]. HBV can remain alive on environmental surfaces for a long time, up to about a week. This ability to stay alive on surfaces makes HBV more capable of producing outbreaks, which continue to occur intermittently in HD centers [5]. HBV transmission between patients and patients-to-staff has been recognized [6].

There has been a significant decline in the burden of HBV in HD patients [7]. Several factors are responsible for this. First HBV vaccination of chronic renal failure and HD patients markedly decreased the rate of infection. Secondly, the routine screening of blood products for HBV and the use of erythropoietin were highly effective in decreasing the spread of HBV infection. Lastly Infection Control measures further decreased the prevalence of HBV in HD

units [8]. These measures included; Use of dedicated dialysis machine for infected patients, routine checking of HBs Ag in patients, the use of personal protective measures, discouraging the use of multi use vials and improvement in environmental cleaning [9]. These measures together lead to 95% decrease in the rates of HBV infection among HD recipients [10].

It is the standard of care to vaccinate all ESRD patients for HBV, preferably prior to starting HD. This response is measured by the titer of protective HBs Ab. A titer above 10 is considered protective [11]. A recent meta-analysis showed that diabetic ESRD patients on HD have even lower response compared to non-diabetic HD patients [12]. Many other risk factors are associated with a worse response to HBV vaccination, including older age, poor nutritional status and HIV or HCV co infection [11].

## Methods

This is a prospective quality improvement initiative to enhance protection against HBV in HD patients. The goal of the study was to estimate the base-line protection against HBV in HD patients. The inclusion criteria include all the in patients with renal failure requiring HD. It included both acute and chronic kidney disease patients. Both

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Received October 21, 2013; Accepted November 13, 2013; Published November 17, 2013

Citation: Singh P, Yassin MH, Lawlor M (2013) Serology for Hepatitis B Virus Inhemodialysis Patients: What is Necessary? J Vaccines Vaccin 4: 210. doi: 10.4172/2157-7560.1000210

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inpatient and outpatient records were reviewed during admission to identify their previous vaccination status. During this period, color coded stickers (indicating the status of HB Ag, HBc Ab and HBs Ab titers) were placed in front of patient 's chart, as part of protocol to enhance vaccination rates in patients with low antibody titers. The following serologies were checked: HBs Ag, HBs Ab titer and HBc Ab total. HBs Ag is done monthly or every new admission. HBs Ab was not checked before 4 weeks after vaccination (false positive is reported). Vaccination was offered to all patients with no evidence of protective HBsAb (titer<10). Engerix 40 mcg was given intramuscular (IM) into the deltoid for patients with HBs Ab titer<10 [13]. The schedule was 0, 1, 2 and 6 months. Recombivax was not available at our facility. We used chi square test and fisher's exact test for statistical analysis.

Primary outcome is to determine the percentage of protected HD patients against HBV. Secondary outcome is to identify ythe risk factors related to low HBs Ab titers. In case of positive HBs Ag or HBc Ab, Infection Control was notified immediately. The vaccination was started during the inpatient stay and a protocol to continue was given to the outpatient HD facility.

Other factors included in this study were age, DM, PVD (based on documented history), albumin levels (checked at time of admission), and hypertension (as defined per Joint National Committee on high blood pressure).

## Results

A total of 59 patients were selected in this study, and out of these, 48 individuals had prior, or current vaccination. Out of the 48 vaccinated patients, 31 were male, and 17 female. 42 patients were ESRD, and 6 had acute renal failure. Out of 48 vaccinated patients, only 29 patients (60.4%) had surface antibody titers in protective range (titers>10). In our study six patients had HCV Ab positive. All 30 non immune patients (29.6%), with surface antibody titers<0 were offered vaccination (Tables 1 and 2).

We also studied correlation of various other factors on the seroconversion after vaccination. Out of vaccinated persons, 42 patients (87.5%) with hypertension were immune (p value 0.03). For patients with DM, 19 patients had protective titers; whereas 11 patients were

found to be non-immune (p value is 0.59). Ten patients with peripheral vascular disease had positive titers and 3 patients had negative antibody titers (p value-0.144). Among the 29 patients with immune titers, the mean albumin was found to be 2.653, with a standard deviation of 0.72. In rest of 19 people without immune titers, mean albumin concentration was found to be 2.731 with standard deviation of 0.9095.

## Discussion

Despite the presence of a potent vaccine, well-defined vaccination guidelines, HBV infection continues to be a problem. HBV is an easily transmissible blood-borne pathogen that is able to produce outbreaks even with low prevalence [5,14,15]. The outbreaks reported in hemodialysis patents are related to multiple factors. Firstly, certain high-risk populations including foreign-born, injection drug users (IDUs) and men who have sex with men (MSM) and acute HD units. Secondly, lack of proof of HBV immune status, as many patients would not be checked for HBs Ab and offer a booster or revaccination series if required. This is a very important issue as HBsAg is frequently checked but HBs Ab is seldom done in many clinical settings. It is obvious that acute HD inpatients are especially vulnerable and also high-risk [16]. Third, a breach in infection control measures most commonly by using multi-use vials [9].

At our inpatient HD unit, one HD patient was found to have positive HBsAg. This initiated surveillance of all patients possibly exposed. This quality improvement project was a recommendation to assure protection and avoid further exposure. In this study, only Sixty percent of patients had HBs Ab titer>10. Interestingly, 6 individuals in this study had positive HBc Ab, which essentially means natural infection with HBV. Out of these 6 individuals, 2 had no protective surface antibody titers (Although HBs Ag was negative).

From our quality study, we were able to detect the low level of immunity for HBV patients. We strongly feel that taking the advantage of inpatient stay to check the HBV serology (HBsAg, HBsAb and HBcAb) unless recently checked is essential. We also feel that vaccination during the inpatient stay and communicating with the outpatient HD unit is essential to prevent unnecessary HBV exposure.

Despite all the efforts to vaccinate HD patients, their response to HBV vaccine is lower and less sustained than healthy individuals [7]. In addition, as per some studies, various factors have been associated with poor seroconversion in these patients. Some of these are DM, low albumin signifying poor nutritional status, and advanced age [17]. Although in this study we couldn't find any statistically significant difference between different possible risk factors.

The recently updated CDC guidelines recommend HBV vaccination of diabetic patients especially less than 60-year-old [17]. It is clearly documented that early vaccination even before HD is associated with better serological response.

## Conclusion

Despite the progress in vaccination, HD patients remain at increased risk of acquiring HBV [15]. This clearly depicts that there is a difference in theory versus clinical practice. There is a need for intense vaccination protocol in HD patients, even early vaccination in ESRD patients, before initiation of HD. No specific risk factors (like DM, low albumin, peripheral vascular disease) were found to be associated with poor response to vaccination in this study. A complete Hepatitis B serology should be checked including HBs Ag, HBsAb, HBc Ab, to

|                             | Immune patients | Non immune patients | p Value |
|-----------------------------|-----------------|---------------------|---------|
| Male                        | 20              | 11                  | 0.316   |
| Female                      | 9               | 8                   | 0.316   |
| Diabetes mellitus           | 19              | 11                  | 0.408   |
| Hypertension                | 28              | 14                  | 0.030   |
| Peripheral vascular disease | 10              | 3                   | 0.137   |

Table 1: Basic characteristics of the vaccinated patients.

|                                    | Immune patients | Non immune patients |
|------------------------------------|-----------------|---------------------|
| Number                             | 19              | 29                  |
| Mean Albumin concentration (mg/dl) | 2.653           | 2.731               |
| a. Std deviation                   | 0.7199          | 0.9095              |
| b. Minimum                         | 1.1             | 1.0                 |
| c. Maximum                         | 4.1             | 4.0                 |
| 25 <sup>th</sup> percentile        | 2.0             | 2.05                |
| 50 <sup>th</sup> percentile        | 2.6             | 2.9                 |
| 75 <sup>th</sup> percentile        | 3.2             | 3.4                 |

Table 2: The numbers mention in the table denotes absolute numbers, except for albumin where it denotes albumin concentration in mg/dL.

screen HD patients, rather than relying solely on HBs Ag. Clearly, there is a critical need for better protection in these patients, and more efforts are needed to vaccinate such patients especially during inpatient visits (supplementary graph).

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