Screening of HBV in Patients of Hemodialysis using HBs Ag in combination with HBc Ab (IgG)

Thesis

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List of Abbreviations

ALT	**:**	Alanine aminotransferase
AST	**:**	Aspartate aminotransferase
CHB	**:**	Chronic hepatitis B
CKD	**:**	Chronic kidney disease
CLD	**:**	Chronic liver disease
CLIAs	**:**	Chemiluminescence immunoassays
DNA	**:**	Deoxy-ribo nucleic acid
dNTPs	**:**	Deoxynucleotide triphosphates
EASL	**:**	European Association for the Study of the Liver
EIAs	**:**	Enzyme immunoassays
ELISAs	**:**	Enzyme-linked immuno-sorbent assays
ESRD	**:**	End stage renal disease
FDA	**:**	Food &drug adminstration
HBcAb	**:**	Hepatitis B core antibody
HBcAg	**:**	Hepatitis B core antigen
HBeAg	**:**	Hepatitis B “e” antigen
HBsAg	**:**	Hepatitis B surface antigen
HBV	**:**	Hepatitis B virus
HCC	**:**	Hepatocellular carcinoma
HCP	**:**	Healthcare personnel
HCV	**:**	hepatitis C virus
HD	**:**	hemodialysis
HIV	**:**	Human immunodeficiency virus
HRP	**:**	Horseradish Peroxidase
IC	**:**	Internal control

IgG	**:**	Immunoglobulin "G"
IgM	**:**	Immunoglobulin "M"
MHL	**:**	Major hydrophilic loop
NA	**:**	Nucleoside or nucleotide analogue
OBI	**:**	Occult hepatitis B virus infection
OHB	**:**	Occult hepatitis B
PBMCs	**:**	Peripheral blood mononuclear cells
PCR	**:**	Polymerase chain reaction
PD	**:**	Peritoneal dialysis
RNA	**:**	Ribo-nucleic acid
SD	**:**	Standard deviation
US	**:**	United states
WHO	**:**	World Health Organization
WP	**:**	Window period

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Introduction

The number of patients with end-stage renal disease treated by maintenance hemodialysis has increased sharply during the last 30 years. Chronic hemodialysis patients are at high risk for infection because the process of hemodialysis requires vascular access for prolonged periods. 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, equipments, environmental surfaces or hands of personnel.

Furthermore, hemodialysis patients are more immunosuppressed, which increases their susceptibility to infection, and they require frequent hospitalization and surgery which increases their opportunities for exposure to nosocomial infections ***(Centers for Disease Control and Prevention, 2007).***

HBV is transmitted by percutaneous (i.e., puncture through the skin) or permucosal (i.e., direct contact with mucous membranes) exposure to infectious blood or to body fluids that contain blood. All HBsAg-positive persons are infectious, but those who are also positive for hepatitis B e antigen (HBeAg) are with high virus titers in their

blood, their body fluids containing serum or blood are potentially highly infectious. HBV is relatively stable in the environment and remains viable for at least 7 days on environmental surfaces at room temperature ***(Alter et al., 2005).***

HBsAg has been detected in dialysis centers on clamps, scissors, dialysis machine control knobs, and doorknobs. Thus, blood-contaminated surfaces that are not routinely cleaned and disinfected represent a reservoir for HBV transmission. Dialysis staff members can transfer virus to patients from contaminated surfaces by their hands or gloves or through use of contaminated equipments and supplies ***(Thompson et al., 2013).***

Once the factors that promote HBV transmission among hemodialysis patients were identified, recommendations for control were established ***(CDC. Hepatitis, 2007).*** These recommendations included: The cornerstone of preventing HBV infection and its sequelae is vaccination, which is recommended for all patients undergoing chronic hemodialysis and the healthcare providers who care for them, Hemodialysis patients are one of the few groups (along with healthcare personnel [HCP]) that are recommended to undergo post-vaccination testing

to assess hepatitis B surface antibody titers, and are the only population recommended to receive booster doses of the vaccine at yearly intervals if their antibody levels have waned. In hemodialysis patients, immunity against hepatitis B cannot be assumed when antibody titers fall below protective levels (typically 10 mIU/ml) ***(Centers for Disease Control and Prevention, 2007).***

Serologic surveillance of patients (and staff members) for HBV infection, including monthly testing of all susceptible patients for HBsAg, isolation of HBsAg-positive patients in a separate room, assignment of staff members to HBsAg-positive patients and not to HBV-susceptible patients during the same shift, assignment of dialysis equipment to HBsAg-positive patients that is not shared by HBV-susceptible patients, cleaning and disinfection of non disposable items (e.g., clamps, scissors) before use on another patient, glove use whenever any patient or hemodialysis equipment is touched and glove changes between each patient (and station); and routine cleaning and disinfection of equipment and environmental surfaces.

The segregation of HBsAg-positive patients and their equipment from HBV-susceptible patients resulted in 70%-

-80% reductions in incidence of HBV infection among hemodialysis patients ***(Alter et al., 2006).***

Several well-defined antigen-antibody systems are associated with HBV infection, including HBsAg and anti-HBs; hepatitis B core antigen (HBcAg) and anti-HBc; and HBeAg and antibody to HBeAg (anti-HBe). Serologic assays are commercially available for all of these except HBcAg because no free HBcAg circulates in blood.

The presence of HBsAg is indicative of ongoing HBV infection and potential infectiousness. In newly infected persons, HBsAg is present in serum 30--60 days after exposure to HBV and persists for variable periods. Transient HBsAg positivity (lasting <18 days) can be detected in some patients during vaccination ***(Lunn ER et al., 2000).*** Anti-HBc develops in all HBV infections, appearing at onset of symptoms or liver test abnormalities in acute HBV infection, rising rapidly to high levels, and persisting for life. Acute or recently acquired infection can be distinguished by presence of the immunoglobulin M (IgM) class of anti-HBc, which persists for approximately 6 months.

In some persons, the only HBV serologic marker detected is anti-HBc (i.e., isolated anti-HBc). Persons in

the latter category include those who circulate HBsAg at levels not detectable by current commercial assays. However, HBV DNA has been detected in <10% of persons with isolated anti-HBc, and these persons are unlikely to be infectious to others except under unusual circumstances involving direct percutaneous exposure to large quantities of blood (e.g., transfusion) ***(Silva et al., 2008).***

Aim of the work

The aim of the present study is to estimate the prevalence of HBV among hemodialysis patients by using HBsAg & detection of possible cases of occult HBV using HBcAb (IgG) in hemodialysis patients if found.