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Post Vaccination Evaluation of Anti-HBsAg Antibody Titers among Haemodialysis Patients

Raj kumar HRV[1], Ramahrishna Devaki[1], Venkataramana Kandi[2,*]

[1]Department of Microbiology, Kamineni Academy of Medical Sciences & Research Centre, L.B.Nagar, Hyderabad, Telangana, India
[2]Department of Microbiology, Prathima Institute of Medical Sciences, Karimnagar, Telangana, India
*Corresponding author: ramana_20021@rediffmail.com

Abstract Hepatitis B virus (HBV) is the second most common viral infection which poses threat of infection among health care workers and those individuals treated for various debilitated conditions in hospital settings. Patients undergoing haemodialysis are at a greater risk of acquiring HBV infection. Although HBV vaccination has been in use for almost three decades, it is not completely certain about its efficacy in long-term protection. Few studies in the past have emphasized the need for evaluation of anti-HBsAg antibody titers among high risk groups that include patients undergoing haemodialysis. Studies in the past have also noted that few vaccinated group do not respond to HBV vaccine and that few other group of vaccinated individuals develop inadequate antibody titers. The present study evaluated the antibody titers among haemodialysis patients and health care workers.

Keywords: *haemodialysis, anti-HBsAg antibody titers, Hepatitis B virus (HBV) infection, non-responders*

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1. Introduction

Among the various viral infections prevalent worldwide, Hepatitis B virus (HBV) infection assumes greater significance due to its high transmissibility especially in health care settings. HBV is second only to human immunodeficiency virus (HIV) infection in terms of potential threat of infection in hospital and to health care professionals. The world health organization (WHO) estimates indicate that 30% of world's population could be infected with HBV. It is also estimated that about 360 million people suffer from HBV chronic infection worldwide and more than six million people die of liver complications each year attributed to HBV infection [1,2]. Prevalence of HBV infection ranges from 2%-10% in various population groups [3]. Although a successful vaccine is available against HBV infection, many people in the developing nations still are not completely vaccinated. Only recently the HBV vaccination has been accepted to be included in the Indian immunization schedule [4]. Among many infectious diseases, viral hepatitis B infection is among the most important challenges faced by health care workers during the management of dialysis patients. The blood-borne hepatitis B virus can be easily communicated in the epidemiological settings of dialysis centers, since susceptible patients are treated in centers together, using extra-corporeal devices and having access to infectious blood. Although there is no need for evaluating healthy vaccinated adult population for the presence of adequate antibody titers, high risk groups including the patients undergoing dialysis are recommended to be tested for antibody titers at least annually [5].

Among the various risk factors contributing to HBV infection, haemodialysis should be considered as significant. Vaccination against hepatitis B for all the patients undergoing haemodialysis is an important method of prevention of HBV infection. In view of the cost associated with HBV vaccine and three doses of vaccine schedule is required to attain adequate and protective levels of antibodies, many individuals in the developing and economically constrained countries still are not properly vaccinated. Although three doses taken successfully in time could be enough and no booster is required, regular evaluation of certain population/risk groups for the presence of protective antibody titers is recommended to minimize the risk of HBV infection [6,7]. Research previously has noted that few vaccinated population (chronic liver/kidney diseases, immunodeficiency due to HIV infection, diabetes mellitus, etc) failed to produce adequate anti-HBsAg antibody titers and are termed as non/poor/hypo-responders. Studies in the past have also reviewed the necessity of evaluating the efficacy of HBV vaccination [8,9]. We studied the anti-HBsAg antibody titers following vaccination against HBV among hemodialysis patients and health care workers attending dialysis clinic.

2. Methods

A total of 381 serum samples obtained from patients attending haemodialysis unit of Kamineni hospitals, Hyderabad formed the study group. The control group comprised of serum samples obtained from 50 staff

members attending dialysis clinic. The study was conducted between January 2010 and December 2011. The Study included two groups; the test group and the control group. 242 (64%) male and 139 (36%) female patients comprised the test group and the control group included 28 (56%) male and 22 (44%) female subjects. All the patients were vaccinated with 40 µg of vaccine at 0, 1, 2 and 6 months. Anti- HBsAg antibodies were detected by ELISA method using "Sandwich Principle" assay (ANTISURASE B-96, General Biologicals Corp., Taiwan) after completion of the vaccination schedule. Anti-HBsAg antibody titers were estimated by drawing graphs using standard sera of strengths 0 mIU/ml, 10 mIU/ml, 100 mIU/ml and 1000 mIU/ml. Sera with titers more than 10 mIU/ml were considered reactive and sera with titers less than 10 mIU/ml were considered non-reactive.

3. Results

Of the total 381 tested, 199 (52%) were found to be reactive and 182 (48%) were observed to be non- reactive. The detailed test result including the age wise distribution is shown in Table 1. Among the 199 positive sera, 95 (48%) had a titter more than 1500 mIU/ml and 33 (17%) were hypo-responders as shown in Table 2. The control group showed 5 non-reactive and 6 with titers higher than 1500 mIU/ml as detailed in Table 2.

Table 1. Age wise distribution of reactivity to HBsAg among the study subjects

AGE (YEARS)	MALES (n=242)		FEMALES (n=139)	
	REACTIVE	NON REACTIVE	REACTIVE	NON REACTIVE
< 10	02	03	00	02
11 – 20	04	02	03	01
21 – 30	18	11	07	11
31 – 40	28	17	14	16
41 – 50	42	30	22	22
51 – 60	24	31	15	15
61 – 70	10	13	06	05
> 70	04	03	00	00
TOTAL	132 (55%)	110 (45%)	67 (48%)	72 (52%)

Table 2. Anti-HBsAg antibody titres among haemodialysis patients and health care workers

TITERS (mIU/ml)	Test (Haemodialysis patients) n (%)	Controls (health care workers) n (%)
NON-Reactive	-	05 (10)
10 – 100	33 (17)	09 (18)
100 – 500	24 (12)	09 (18)
500 – 1000	31 (16)	14 (28)
1000 – 1500	16 (08)	07 (14)
> 1500	95 (48)	06 (12)
TOTAL	199	50

Of the reactive patients, 48% had anti-HBsAg antibody titers more than 1500 mIU/ml suggesting a good immunity against HBV (Responders). 33 patients had anti-HBsAg antibody titers between 10 – 100 mIU/ml showing hypo-responsiveness (hypo-responders). Sero-conversion rate was better in males (66%) as compared to females (34%). Among the staff members tested, 90% were reactive for anti-HBsAg antibodies. 9 (18%) members had titers between 10 – 100 mIU/ml.

4. Discussion

HBV virus is distributed worldwide showing 9 genotypes. It has been observed that "a" component of HBV is common among all genotypes and that HBV with "D" genotype was found to be showing intrinsic resistance towards antiviral agents [10]. The present study results have shown that 182 (48%) of vaccinated population undergoing haemodialysis were non-responders. Among the 199 (52%) subjects showing detectable antibody titers, 33 (17%) had titers between 10 IU/L and 100 IU/L. Study has also revealed that 5 (10%) of the health care workers were having antibody titers less than 10 IU/L. These observations indicate the need for evaluation of antibody titers among population groups which have potential risk of developing infection in future.

According to the center for disease control and prevention's (CDC) advisory committee on immunization practices (ACIP), HBV immunization is recommended to all individuals preferably immediately after birth [7]. Anti-HBsAg antibody titer more than 10 IU/L of blood indicates protective sero-conversion after vaccination [11]. Previous research study has observed that individuals with titers above 100 IU/L remain protected for a very long time and may not require further doses of vaccine and that in vaccinated people with titers between 10 IU/L and 100 IU/L should be closely observed and a booster might be given to avoid future infection [12].

It has been noted that 50% population who received immunization in the childhood were not having protective antibody titters signifying the importance of evaluating the antibody titters at least among the risk groups and those who have been vaccinated for more than 10 years. It has also been found that 78% of individuals vaccinated at birth were having protective antibody titters. Among those who were having protective antibody titers, only 45% had titers more than 100 IU/L [13].

Recent research has also noted that high dose vaccination and a birth weight more than 2000g could positively influence the success of vaccination and vice versa [14]. Previous research has also recommended that there is no need to give booster vaccine dose even in those individuals with antibody titters varying between 10 IU/L and 100 IU/L considering the fact that immunological memory could initiate protective immunity [15,16].

Study in the past has also observed that about 5-10% of vaccinated population may turn out to be non-responders. It was also observed that in some people the protective immunity may gradually wane over 10 years and some HBV infected individuals may suffer from chronic infection signifying the need for evaluation of antibody titters and giving booster vaccine doses if needed [17]. Although it is still unclear as to what could be the exact reasons behind the failure to respond to the vaccine, recent studies have noted that few individuals might be genetically predisposed [18]. Previous research studies have observed that non-functioning of human leukocyte antigen (HLA) and class II major histocompatibility complexes (MHC-II), and failure to mount an immunological response to viral antigens could contribute to vaccine non –responsiveness [19,20].

European consensus group on HBV infection/vaccination has observed that there is a need for regular evaluation of anti-HBsAg antibody titters in select population groups

which included haemodialysis patients and also to recognize non-responders. This would be instrumental to review the current immunization policies and implement corrective measures [21].

There are contrasting observations made by previous studies where in few studies recommend that a booster vaccine dose is not required in most vaccinated groups and that individuals could be protected for more than 10 years after vaccination [22,23,24].

Few other research studies indicate that although HBV vaccination at birth confers long-term immunity to HBV infection and carriage, they have noted that the antibody titres may gradually wane and could pose a potential risk of future infection [25,26].

In spite of using high dose vaccine, some patients of end stage renal disease do not develop adequate antibody titers [27,28]. The factors implicated for poor response of hemodialysis patients to hepatitis B vaccine include and may not be limited to uremia, malnutrition; as indicated by a low albumin and pre-dialysis urea, low body weight, diabetes mellitus, old age, sero-positivity for antibody against hepatitis C virus (HCV), impaired T-cell receptors expression and expression of HLA DR3, DR7, and DQ2. In this regard the usage of vaccine adjutants like Granulocyte-macrophage colony-stimulating factor (GM-CSF); incorporation of pre S protein (Pre S1 and Pre S2) components which increases the sero-conversion rate in the vaccine groups; employing other methods of injecting the vaccine like via intra dermal route/oral vaccination or developing new vaccine can be the possible alternatives for increasing the responsiveness to the vaccines [29].

5. Conclusion

In conclusion it must be noted that not all HBV vaccinated individuals develop protective antibody titres. Few vaccinated people may remain as non-responders and few others have insufficient antibody titres. Although studies have observed that moderate level (10 IU/L -100 IU/L) antibodies are present in people who were vaccinated for 10 years and immunological memory could still prevent future HBV infection, risk of HBV infection cannot be completely ruled out. HBV vaccine status and the presence of protective antibody titres should be regularly evaluated in high risk groups including the haemodialysis patients and health care workers and a booster dose vaccine are given to prevent future HBV infection and related complications.

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