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ANTIBODY TITERS FOLLOWING HEPATITIS B VACCINATION IN HEALTH CARE WORKERS IN KHARTOUM STATE, SUDAN

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ABSTRACT

Hepatitis B vaccination is the most effective measure to prevent HBV infection and its consequences. The best strategy to eradicate HBV infection is a universal vaccination program. This study was a descriptive cross sectional study aimed at evaluating the efficiency of HBV vaccine in term of anti-HBs Ab level among vaccinated health care workers (HCWs) in Bahri Teaching Hospital, Khartoum state, Sudan. Ninety HCWs agreed to participate in this study, HBV antibody level (quantitative antibody) against HBsAg were measured using ELISA technique. The majority of study population 66 (73.33%) were aged (21-30 years), the active age groups (21-30) and (31-40) revealed remarkable reduction of HBsAb titer, 29 (43.93%) and 11 (55%), respectively. A total of 49 (54.4%) participants showed antibody titers above 10 IU/mL, 14 (15.6%) of them revealed strong response with anti-HBs Ab titers >100 IU/mL while HBsAb titers less than 10 IU/mL was detected in 41(45.6%) participants. A total of 83(92.22%) of the study population had the vaccine dose at proper interval whereas 7(7.78%) had the vaccine at irregular time. Eighteen18 (27.3%) of the participants who had the vaccine less than 5 years ago and 22 (91.7) of candidates who received the vaccine more than 5years ago did not respond to vaccine. Sixty-six (66; 73.33%) of the entire participants were females and 24 (26.67%) were males, out of which 28(42.2%) and 13(54.2%) of male and female, respectively fail to develop anti-HBsAb titer 10 IU/mL. ***Conclusion****: this study revealed that other non immunological factors influence the outcome of vaccination; interval after vaccination and chronic disease were found to be significantly correlated (P<0.05) with antibody titers following hepatitis B vaccination.*

Keywords: Health care workers, HBV antibody titers, Hepatitis B vaccine.

Contribution/ Originality

This study contributes in the existing literature regarding the importance of checking the post vaccination status of HCWs as it ensure safety of employee, reduces rate of transmission and functioning as a cost effective exercise at individual as well as national level.

1. INTRODUCTION

Viral hepatitis is a systemic disease primarily involving the liver. It's one of the most common viral diseases affecting man. Infection with hepatitis B virus (HBV) leads to a wide spectrum of clinical presentations ranging from an asymptomatic carrier state to self-limited, acute or fulminant hepatitis to chronic hepatitis with progression to cirrhosis and hepatocellular carcinoma. Both viral factors as well as the host immune response have been implicated in the pathogenesis and clinical outcome of HBV infection [1]. Despite the fact that the introduction of Hepatitis B vaccination as helped in reducing the incidence of the infection, it is important that the immunologic response to the vaccine be assessed.

There is no seasonal trend for HBV infection and no high predilection for any age group, although there are definite high-risk groups such as parenteral drug abusers, institutionalized persons, health care personnel, multiply transfused patients, organ transplant patients, hemodialysis patients and staff, highly promiscuous persons, and newborn infants born to mothers with hepatitis B. Worldwide, one million deaths per year are attributed to HBV-related liver disease and hepatocellular carcinoma [2].

Health care workers HCWs (medical and dental surgeons, pathologists, other physicians, nurses, laboratory technicians, and blood bank personnel) have a higher incidence of hepatitis and prevalence of detectable HBsAg or anti-HBsAg than those who have no occupational exposure to patients or blood products [3]. It has been estimated that 600,000 to 800,000cut and puncture injuries occur among the HCWs per year, of which approximately 50% are not registered. Needle stick injuries among health care workers (HCWs) are a well-recognized health hazard that causes transmission of viral infections, especially hepatitis B virus (HBV).The risk of contracting hepatitis B by healthcare personnel is four times greater than that of the general adult population [4].

In terms of public health, the best strategy to eradicate HBV infection is a universal vaccination program as recommended by WHO. Implementation of a universal vaccination program is highly desirable, particularly among high-risk situations that might not be adequately addressed by mass vaccination programs such as person who perform tasks involving contact with blood, blood-contaminated body fluids, other body fluids, and sharps [5, 6]. Hepatitis B vaccine can be administered at the same time as other vaccines with no interference of antibody response to other vaccines [5]. About 5-10% of those vaccinated against HBV fail to respond with development of antibody to the HBV [7, 8]. However, the health care workers vaccinated against HBV infection and do not develop immunity remain at high risk of being infected.

A vaccine for hepatitis B has been available since 1982. The initial vaccine was prepared by purifying HBsAg associated with the 22-nm particles from healthy HBsAg-positive carriers and treating the particles with virus-inactivating agents [9]. Currently, recombinant HBsAg is used for HBV vaccination, and the development of antibody to HBsAg is typically associated with protective immunity. The core open reading frame encodes a polypeptide that is expressed as either the hepatitis B e antigen (HBeAg) or the viral capsid protein (HBcAg) [10]. These vaccines are administered by the intramuscular route in the deltoid muscle and are highly immunogenic, inducing a protective anti-HBs antibody titer (>10 IU per mL) in more than 95% of healthy children or young adults [11]. Two schedules of administration are approved:

(a) Three initial injections at 1-month intervals and a booster at 12 months.

(b) Two initial injections 1 month apart, followed by a booster at 6 months.

The HBV vaccine is associated with rare side effects, most commonly pain or soreness at the injection site. Neurologic disorders such as multiple sclerosis and transverse myelitis have not been causally linked to the HBV vaccine.

Sudan is considered highly endemic for HBsAg, with prevalence about 16%–20% in the general population. In a study conducted in Omdurman (Khartoum state) among adults with acute hepatitis, HBV infection was 12.6% [12].

Hence, the present study aimed to evaluate the immunologic of hepatitis B virus vaccine among vaccinated Sudanese health care workers in term of anti-hepatitis B surface antigen level and to determine the factors affecting the vaccination.

2. MATERIAL AND METHODS

2.1. Ethical Consideration

The ethical consideration of this study was approved by ethics committee, faculty of graduate studies, Alzaeim Alazhari University, Sudan. The participants were informed about the purpose of the research before sample collection, and verbal or signed consent obtained from them. Privacy and confidentiality of participants were ensured.

2.2. Type of Study and Sample Size

The present study was a descriptive cross sectional study, which covered vaccinated health workers in Bahri Teaching Hospital, Khartoum state Sudan. Convenience sampling techniques were used; (90) HCWs agreed to participate in this study.

2.3. Inclusion Criteria

Apparently healthy health care workers who were vaccinated against HBV and had no history of HBV infection or received hepatitis B immunoglobulin prophylaxis were included.

2.4. Exclusion Criteria

Health care workers who were not vaccinated or vaccinated but had history of HBV infection or received hepatitis B immunoglobulin prophylaxis were excluded.

2.5. Tools of Data Collection

Data of some demographic factors such as gender, age, weight, interval after vaccination, regulation of vaccine doses, history of chronic disease (blood pressure, diabetes, other), were collected using direct interview approach.

2.6. Laboratory Method

2.6.1. Sample Collection

Sterile disposable vacutainer tube was used to collect 5 ml of blood from the anticubital vein under aseptic conditions and the blood samples allowed to clot at room temperature. The clotted samples were centrifuged at 5000 rpm for 10 minutes in order to separate the sera; the obtained sera were frozen at -20°C until analyzed.

2.6.2. ELISA Technique Procedure

HBs antibody level (quantitative antibody) against HBsAg were measured using ELISA technique, briefly:

- Two negative controls and two positive controls were used.
- 0.05 ml of each serum sample was applied to separate well of microplate using automated pipette.

The conjugate was supplemented to each well of microplate and the plate incubated at 37°C for 60 min for Ag-Ab complex.

- After incubation period the microplate plate was washed five times in ordered to remove the uncombined Abs.
- 0.05 ml of reconstituted substrate (A and B) was applied to microplate and incubated at 37°C for 10 mins.
- Finally, 0.05 ml of stopped solution was added to each well of microplate.

2.6.3. Reading and Interpretation of the Results

The optical density (OD) of microplate was obtained at the 450 nm. The presence or absence of antibody to hepatitis B surface antigen was determined by comparing the absorbance measured for each sample to the calculated cut- off value.

According to the measured anti-HBs Ab level, the participants were classified into three groups:

Non responders: anti-HBsAb level ≤ 10 IU/mL.

Acceptable responders: anti-HBsAb level of 10-100 IU/mL.

Good responders: anti - HBsAb level of ≥ 100 IU/mL.

The protection level was considered when anti-HBsAb titers were above 10 IU per mL [13].

2.7. Method of Data Analysis

Analysis of results was carried out by means of the statistical package for the social sciences (SPSS). A descriptive statistic frequency and Chi-square were used to compare the variables with seropositive results. P value <0.05 considered significant.

3. RESULTS

Ninety health care workers vaccinated against hepatitis B virus participated in this study in order to determine the efficiency of HBV vaccine in terms of anti-hepatitis B surface antigen level and to determine the factors affecting the vaccination among Sudanese health care workers. The majority of the HCW 66 (73.3%) were within theage range of 21-30 years, the active age groups (21-30) and (31-40) revealed remarkable reduction of HBsAb level which was 29 (43.9%) and 11 (55.0%), respectively. Most of study group participants (57; 63.3%) were within the weight range of 51-70 kg. The participants of weight more than 90 kg 4 (100%) did not respond to vaccine. Just 49 (54.5%)_of the participants had antibody titers above 10 IU/mL, 14 (15.6%) of them had anti-HBs Ab titers >100 IU/mL while the HBsAb titers less than 10 IU/mL was detected in_41(45.6%) {Table1}. Eighty-three (83; 92.2%) of study population had the vaccine doses at regular interval whereas 7(7.8%) had the vaccine at irregular time. None of the participants7 (100%) who were vaccinated at irregular interval had antibody titers_>100 IU/mL and 4 (57.1%) of them failed to develop immunity i.e anti-HBsAb titers >10 IU/mL. Twenty-two (22; 91.7%) of the participants got the vaccine more than five years before the study and they displayed less reactivity than those vaccinated less than five years. Similarly, all the participants 4(100%) which had chronic disease did not respond to vaccine while 37(43.0%) of the healthy participants were below the protective level. None of the participants 90 (100%) had taken the booster dose. Sixty-six (66; 73.3%) of the participants were females and 24 (26.7%) were males, with 28(42.2%) and 13(54.2%) of male and female, respectively fail to develop anti-HBsAb titers >10 mIU/mL {Table 1}.

These results indicated statistically significant association between response to HBV vaccine (anti HBV Ab >titer 10 IU/ml) and interval after vaccination(P<0.05) and chronic disease(P<0.05).

4. DISCUSSION

The present study involved 90 Sudanese HCWs vaccinated against HBV infection and subjected to the determination of anti-HBsAb titers, and factors affecting HBV vaccination.

The results revealed low protective level of HBV antibody among Sudanese health care workers, of which 49 (54.44%) of the participants acquired antibody titer higher than 10 IU/ml. Contrary to this finding, the protective level among HCWs was high in Egypt (96%) [14], Iran (88.1%) [15] and Pakistan (86%) [16]. However, Abe, et al. [7], Xiao-wen, et al. [8] and Kane, et al. [17] reported that about 5-10% of those vaccinated people fail to develop antibody to the vaccine. Several factors relating to the non-response exhibited by the participants have been

identified, which include genetic factors, age older than 40 years and high body mass index. More so, patients who are immunosuppressed or on renal dialysis may respond less and require larger or more frequent doses of vaccine. Poor responses are also associated with obesity and alcoholics, especially if they are with advanced liver disease [18]. However, in our study the less reactivity could not be attributed to a particular age range (*P* value 0.530), as the active age group (less than 40 years) showed remarkable none response. This result not in accordance with the reports of Tohme, et al. [19] results, who evaluated the seroprotection conferred by hepatitis B vaccine among older adults. Their reports stated that age was a significant determinant of seroprotection conferred by Hepatitis B vaccination, therefore the failure to response to HBV vaccine in our study could be related to lack of follow up after vaccination since none of the participants (90; 100%) got booster dose. More so, the interval after vaccination showed significant statistical relation (*P* value 0.001); the participants who received the vaccine more than five years before the study displayed less reactivity than those vaccinated less than five years, this finding indicated that HBsAb titer may decrease over time after vaccination,which is in agreement with the reports of Platkov, et al. [20] and Hosseini, et al. [21]. They reported that the post vaccine titers are in linear dependence on the time elapsed since the vaccination. Also the present study displayed significant relation between response to vaccine and systemic disease (*P* value 0.048); none of participants who had systemic disease responded to vaccine; which point out that some other non immunological factors (obesity and chronic disease) influence the outcome of vaccination. Furthermore, the participants who had the vaccine doses at irregular time showed less reactivity than others who received the doses at regular interval according to vaccination schedule (*P* value 0.106).

In the present study, the female showed less response to HBV vaccine (54%) than male (42.42%), however statically there was insignificant relation ($P>0.05$). Similar results were reported by Zeeshan, et al. [16] at Pakistan and this could be related to genetic factors.

5. CONCLUSION

There is a need to strictly implement policy for hepatitis B immunization among the health care setting in developing countries. Furthermore, it is essential to check the post vaccination status of all HCWs as it does not only ensure safety of employee but also reduces rate of transmission, hence functioning as a cost effective exercise at individual as well as national level.

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Table-1. showed frequency and statistical relation of antibody titers (IU/ml) following Hepatitis B vaccination in Health Care Workers in Khartoum state, Sudan

no	Factors		Antibody titres IU/ml						Total	%	*P* value
			<10		10-100		>100				
			Frequency	%	Frequency	%	Frequency	%			
1	Age group/year	21-30	29	43.9	27	40.9	10	15.2	66	73.3	0.530
		31-40	11	55.0	8	40.0	1	5.0	20	22.2	
		41-50	1	25.0	00	00.0	3	75.0	4	4.40	
		Total	41	45.5	35	38.8	14	15.5	90	100	0.109
2	Weight/kg	< 50	4	30.8	9	69.2	00	00.0	13	14.4	
		51-70	24	42.1	21	36.8	12	21.1	57	63.3	
		71-90	9	56.3	5	31.3	2	12.5	16	17.8	
		>90	4	100	00	0.00	00	0.00	4	4.40	
		Total	41	45.6	35	38.9	14	15.6	90	100	
3	Interval after vaccination/year	< 5	18	27.3	33	50.0	15	22.7	66	73.3	0.001
		>5	22	91.7	2	8.30	0	0.00	24	26.7	
		Total	40	44.4	35	38.9	15	16.7	90	100	
4	Sex	male	28	42.4	28	42.4	10	15.2	66	73.3	0.577
		femal	13	54.2	7	29.2	4	16.6	24	26.7	
		Total	41	45.6	35	38.9	14	15.6	90	100	
5	Chronic disease	yes	4	100	00	000	00	000	4	4.40	0.048
		no	37	43	35	40.6	14	16.2	86	95.6	
		Total	41	45.5	35	38.8	14	15.5	90	100	
6	Vaccined at schedule	Yes	37	44.5	32	38.5	14	16.8	83	92.2	0.106
		no	4	57.1	3	42.8	00	00	7	7.8	
		Total	41	45.5	35	38.8	14	15.5	90	100	

- Chi-square was use to calculate P value.
- P value <0.05 consider significant.