STUDY OF IMMUNISATION STATUS BY ESTIMATION OF ANTI-HBS ANTIBODY IN POST HEPATITIS B VACCINATED INDIVIDUALS

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ABSTRACT

BACKGROUND

Hepatitis B Virus (HBV) infection is a major public health problem in India. Hepatitis B can be prevented by hepatitis B vaccine, which is the first anticancer vaccine, because it can prevent a form of liver cancer. The protective antibodies induced by vaccination wane gradually over period of time.

The aim of the study is to-

1. Estimate serum levels of anti-HBs in individuals vaccinated with hepatitis B vaccine.
2. Immunisation status of hepatitis B vaccination in individuals.

MATERIALS AND METHODS

A serological study was carried out from March 2015 to the end of September 2016 aimed at estimating the level of HBs-antibody. Total of 330 individuals from healthcare workers, staff and children who have received full course of hepatitis B vaccine were selected for study. In a cross-sectional study, anti-HBs antibody was determined by Enzyme-Linked Immunosorbent Assay (ELISA) method.

RESULTS

Three hundred and thirty individuals were enrolled in the study, out of which, 136 were men and 194 were women. Majority were in the age group 20 to 40 years. Anti-HBs antibody titre was more than 100 IU/L in 74% individuals. Titre was between 10 IU/L-100 IU/L in 16% individuals. Anti-HBs titre was less than 10 IU/L in 10% individuals. There was a significant decline in the levels of antibody overtime post vaccination. Antibody titre was low in individuals with diabetes mellitus. Low antibody titre was noted in smokers.

CONCLUSION

In this study, majority had desirable immune response to the HBV vaccine. Diabetes mellitus, long duration post vaccination and positive smoking history have attributed to low anti-HBs titre in subjects who had inadequate levels in our study. As immunological memory persists for long time even in the absence of significant titre of anti-HBs, booster dose vaccination is routinely not advocated for general population. But, healthcare professionals are advised to receive booster dose vaccination at 5 years if anti-HBs value is less than 10 IU/L. Study recommends periodic monitoring of anti-HBs assay.

KEYWORDS

Anti-HBs; Hepatitis B Virus; Immunity.

HOW TO CITE THIS ARTICLE: Lakshmanan KP, Bhaumik P, Sarkar P, et al. Study of immunisation status by estimation of anti-HBs antibody in post hepatitis B vaccinated individuals. J. Evid. Based Med. Healthc. 2017; 4(79), 4656-4660. DOI: 10.18410/jebmh/2017/931

BACKGROUND

It is estimated that about one third of the world's population has been infected with Hepatitis B Virus (HBV). Of which, 400 million are believed to be chronic carriers. Approximately, one million deaths each year are attributable to HBV complications including hepatocellular carcinoma, liver cirrhosis, chronic and acute hepatitis. HBV associated chronic carrier ship is highest in India.[1] Prevalence rate of hepatitis varies from 1 to 13 percent with an average of 3.7%. There are 45 million Hepatitis B Virus (HBV) carriers in India. Every year, one million Indians are at risk for HBV and about 1,00,000 die from HBV infection.[2]

Hepatitis B vaccine provides protection against infection with HBV by producing immunity or antibodies to the surface protein or outer coat of the virus.[3] Under the Universal Immunisation Programme, Government of India, is providing vaccination to prevent eight vaccine preventable

Financial or Other, Competing Interest: None.
Submission 15-09-2017, Peer Review 22-09-2017,
Acceptance 31-09-2017, Published 02-10-2017.
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DOI: 10.18410/jebmh/2017/931

diseases nationally, i.e. diphtheria, pertussis, tetanus, polio, measles, severe form of childhood tuberculosis and hepatitis B and meningitis and pneumonia caused by haemophilus influenza type B and against Japanese encephalitis.[4]

The road to the hepatitis B vaccine began in 1963 when American physician/geneticist Baruch Blumberg discovered Australia antigen in the serum of an Australian Aboriginal person.[5] Later in 1986, second generation vaccines mainly recombinant non-glycosylated proteins were developed by inserting the HBV gene that codes for the surface protein into the yeast Saccharomyces cerevisiae.[6] Recently, third generation vaccines produced in mammalian Chinese Hamster Ovary (CHO) cells[7] have been shown to induce an immune response, which occurs earlier and is stronger. Even in many so called "non-responders" to S protein a protective immune response was induced. Hepatitis B vaccine is recommended for unvaccinated adults, who are at risk for hepatitis B virus infection[8] including-

- People whose sex partners have hepatitis B.
- Men who have sexual contact with other men.
- People who share needles, syringes or other drug-injection equipment.
- Healthcare and public safety workers at risk for exposure to blood or body fluids.
- People with chronic liver disease, kidney disease, HIV infection or diabetes.

The standard recommended regime is three intramuscular doses at 0, 1 and 6 months[9] in the deltoid muscle. Anti-HBs estimation after vaccination is recommended for healthcare workers and public safety workers at high risk for continued percutaneous or mucosal exposure to blood or body fluids to guide post-exposure prophylaxis, chronic haemodialysis patients, HIV-infected persons, sex partners of HBs Ag-positive persons and other immune compromised persons and for follow-up.[10] Testing should be performed 1 month after administration of the last dose of the vaccine series using a method that allows determination of a protective concentration of anti-HBs.

Many studies and research works have been done on the basis of estimation of antibody to hepatitis B antigen. But, most of the available data on the immunisation status is from western literature. The need for the present study is becoming increasingly important as the number of hepatitis B positive individuals are building up regularly. In most of the times, healthcare professionals are in constant exposure to blood and blood products from these patients. This carries a potentially higher risk of acquiring hepatitis B infection.

Various factors are responsible for the differences in immunisation status of individuals who have received full course of hepatitis B vaccine. This study aims to find out the level of anti-HBs in hepatitis B vaccinated individuals to measure an existing protection.

MATERIALS AND METHODS

The study comprised of 330 individuals from healthcare workers, staff and children who have received full course of hepatitis B vaccine. The cross-sectional study was conducted from March 2015 to September 2016. Ethical clearance from the institutional ethical committee and Informed consent from individuals were obtained. After checking the vaccination card, anti-HBs was measured by Enzyme Linked Immune Sorbent Assay (ELISA) test.[11]

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.

RESULTS

Three hundred and thirty individuals were enrolled in the study. There were 194 (59%) females and 136 (41%) males. Hepatitis B vaccine recipients were divided into three groups-

1. Non-responders have peak anti-HBs levels of ≤10 IU/L.
2. Low responders have peak anti-HBs levels of 10-100 IU/L.
3. Good responders have peak anti-HBs levels of ≥100 IU/L.[12]

Since, our study group involves high-risk individuals, serum anti-HBs level less than 10 IU/L was considered as inadequate.

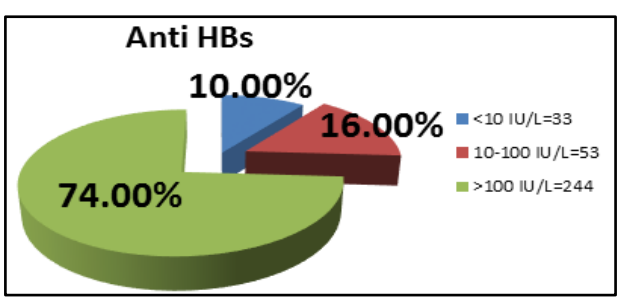

Figure 1. Anti-HBs Titre in Study Population

The mean age of the study population was 33.5 years. 139 individuals (40%) have received full course of hepatitis B vaccine more than 10 years ago. Out of the 330 individuals, 33 had history of diabetes mellitus, 36 of them had history of hypertension. From the study sample, it was observed that 49 individuals were smokers.

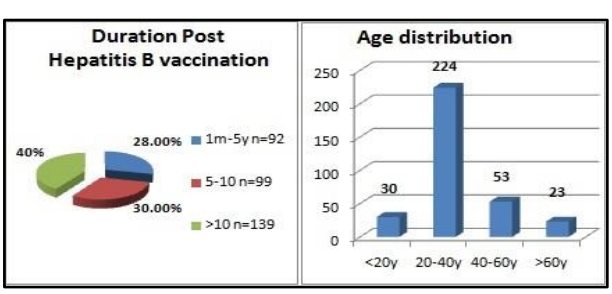

Figure 2. Duration Post Hepatitis B Vaccination and Age Distribution

Analysis- The study revealed that majority of the individuals were in age group of 20-40 years. Anti-HBs

antibody titre was estimated across various age groups. It is found that the anti-HBs antibody titre reduces as the age increases (p-0.0001).

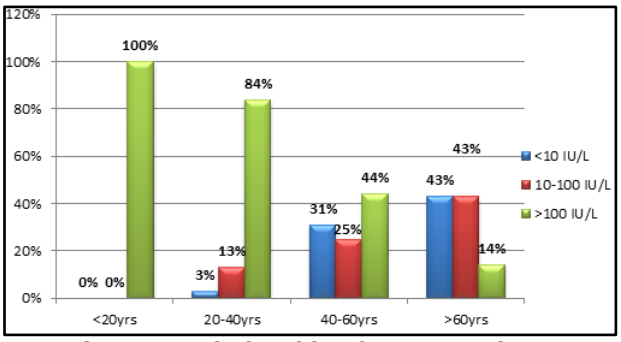

Figure 3. Relationship of Age to Anti-HBs

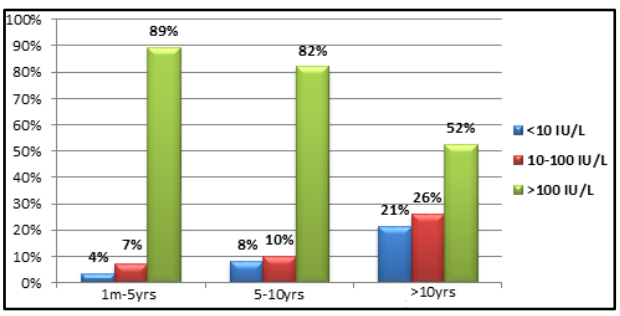

Figure 4. Relationship of Duration Post Vaccination to Anti-HBs

From the table, it is evident that longer the duration post vaccination, lesser is the anti-HBs titre (p-0.0001).

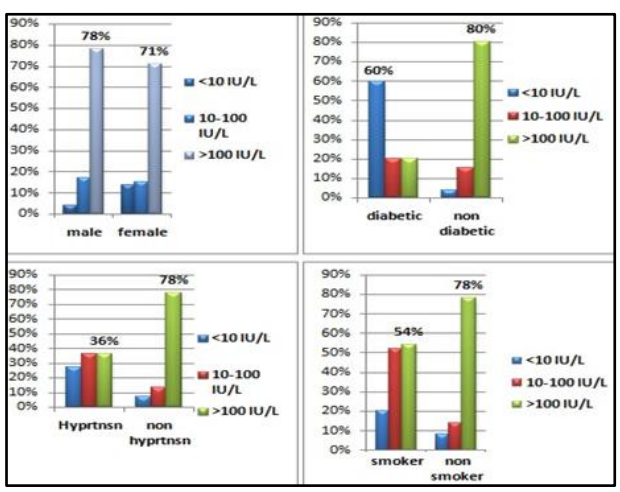

Figure 5. Other Factors in Comparison with Anti-HBs

Anti-HBs titre is less in patients who are diabetic (p-0.0001). It is observed that the hypertensive subjects also have less anti-HBs titre as compared to non-hypertensive (p-0.008). The study revealed that the antibody titre was less in smokers; however, the 'p' value was not significant (P value- 0.113).

DISCUSSION

Hepatitis B is the most important infectious occupational disease for the healthcare workers. The high risk of being infected is the consequence of prevalence of virus carriers in the assisted population. The high frequency of exposure to blood, body fluids and the high contagiousness of hepatitis B virus. Immunisation and post exposure management are among the integral components of complete infection control programme[13] for healthcare workers.

Majority of studies have reported a 90% reduction of the anti-HBs level in the first 24 months, followed by a much slower decline[14] during the later period. Antibody levels more than 100 IU/L are considered to be protective. Antibody level less than 10 IU/L considered inadequate and are candidates for booster dose of vaccination especially for healthcare personnel.[15]

Age- In present study, anti-HBs was estimated in various age group individuals and found that younger the individual, more is the antibody titre. 43% individuals who are more than 60 years have antibody titre less than 10 IU/L.

		Age			
		<20	20-40	40-60	>60
Anti-HBs	<10 IU/L	0	7	17	10
	Total individuals	**30**	**224**	**53**	**23**
	Percentage	**0%**	**3%**	**32%**	**43%**

Table 1. Anti-HBs Distribution in Various Age Groups

Floreani A, Baldo V[16] et al conducted a study in 2004 to evaluate the long-term persistence of seroprotection after Hepatitis B Virus (HBV) vaccination and concluded that rate of persistence of anti-HBsAb of vaccinated individuals had been decreased by age. Aghakhani A, Banifazl M et al[17] conducted a study in 2011 to detect the persistence of antibody to hepatitis B surface antigen among vaccinated children in a low hepatitis B virus endemic area and concluded that vaccine-induced anti-HBs titre diminish to low or undetectable levels with age.

Duration Post Vaccine- In the current study, antibody level against HBV declined significantly overtime. Antibody titre was less than 10 IU/L in individuals vaccinated more than 10 years ago.

		Duration Post Vaccine		
		1 month - 5 years	5-10 years	>10 years
Anti-HBs	<10 IU/L	4	8	15
	Total	**92**	**99**	**139**
	Percentage	**4%**	**8%**	**21%**

Table 2. Anti-HBs According to Duration Post Vaccination

In some studies[18] from Taiwan, anti-HBs level 7-20 years after vaccination ranged from 50.5-77%. In these studies, a "waning-off" effect of anti-HBs seropositivity acquired from the hepatitis B vaccination program has been observed. In a series of studies among healthy children who had received a complete HBV immunisation program, protective anti-HBsAb levels were gradually declined after the last dose of vaccine.[19]

The declining trend of anti-HBs levels, which was reported in this study and the diversity of results in different

studies maybe largely attributed to differences in the environmental and genetic factors, type and dose of the vaccines, age of initial vaccination, schedule of immunisation and intervals between vaccine administrations. Chadha[20] studied the long-term persistence of anti-HBs and concluded that persistence of immunological memory remains for at least 10 years.

Sex- The results of the current study in comparison with other studies revealed no significant difference regarding gender and anti-HBs levels. Baghianimoghadam MH, Shadkam MN et al found that anti-HBs production was not affected by sexual factors such as feminine hormones.[21] This could be attributed to small sample size. Studies with larger sample size only can help to draw conclusive remarks.

Diabetes- According to the quantification of the anti-HBs titre tests, among the 297 nondiabetic individuals, 15 (5%) individuals had anti-HBs <10 IU/L. Among the 33 diabetic individuals, 20 (60%) individuals showed anti-HBs <10 IU/L. This difference in anti-HBs response between healthy and diabetics was significant (p 0.0001). Heba Elrashidy, Ashraf Elbahrawy[22] et al conducted a study and found that, that diabetic individuals display significantly decreased levels of anti-HBs in comparison to healthy control children.

The poor immune response of IDDM patients to HB vaccination maybe linked to defects in antigen uptake, processing and presentation as well as suppression of B-cell production of the anti-HBs.[23]

Smokers- In the current study, 10 of the 49 smokers showed antibody titre below 10 IU/L, this accounts to nearly 20.4%. This is consistent with decreased antibody titre noticed in smokers in other studies. Cigarette smoking is associated with range of alterations in immune function. It has been supposed, the diminished response in smokers maybe due to the increasing of T suppressor lymphocytes.[24]

Healthcare workers at risk who have antibody levels below 10 IU/L are advised to receive booster injections[25] with the aim of providing protective immunity/protection against significant breakthrough infection. All the study subjects were informed about their anti-HBs titre and were informed to assess their anti-HBs periodically.

SUMMARY

A cross-sectional study of 330 subjects who received full course of hepatitis B vaccination at varied time intervals was done. Antibody to hepatitis B virus surface protein (anti-HBs) was estimated in these individuals.

The study showed that the anti-HBs titre was more in younger individuals when compared to older individuals.

It is obvious from the current study that that vaccine-induced anti-HBs levels decline to low levels with increase in the duration of post vaccination. Anti-HBs titre being high in early post-vaccination period compared to the low levels of titre in individuals vaccinated more than 10 years ago.

There was no significant variation in anti-HBs titre among men and women. In the current study, the long-term seroprotection rate after HB vaccination was significantly reduced in diabetes mellitus. Schillie et al found an association between anti-HBs response and duration of DM as well as glycaemic control. Tobacco smoking was found to be associated with low anti-HBs titre.

Loss of anti-HBs does not necessarily mean loss of immunity as the immunologic memory induced by the HBV vaccine persists even as anti-HBs decline. It is said that the persistence of immunological memory remains for at least 10 years. However, for a high-risk group population such as medical students and residents, who are at continuous exposure to HBV, it is reasonable to determine the anti-HBs response at one month post vaccination. In order to confirm the persistence of immune protection, anti-HBs titre is measured 5 years after the last inoculation. Study recommends periodic monitoring of anti-HBs assay for all healthcare workers. Booster doses are considered for individuals with anti-HBs levels less than 10 IU/L. Yearly, anti-HBs estimation is essential for individuals receiving regular blood transfusion, immunosuppressed individuals, chronic kidney disease individuals, individuals on long-term corticosteroids and booster dose advised based on anti-HBs levels.

CONCLUSION

It was observed that findings were almost in accordance with studies conducted earlier. The present study emphasises on assessment of anti-HBs level after vaccination against HBV. The study shows that young healthy individuals without any contributing factors likely to have adequate anti-HBs titre in the early post vaccination period. Seroprotection rate after HBV vaccination was high one month after the third dose and then declined gradually overtime. Further follow-up is therefore needed to determine the need for booster dose based on anti-HBs levels.

Limitations

The present study was carried out over a period of one year and included a modest sample size of 330 subjects. Other studies on larger scales including those from general population conducted over longer time periods are required to properly validate the findings of this study.

Individuals were selected in random depicting only a small section of the society.

Most of the studies involving HBV antibody titre were prospective nature with sample analysis being carried out at different intervals. Our study however was cross sectional in nature and antibody analysis was done only at one point of time.

However, this study will be considered as a foundation stone for further studies, which can be conducted over long period of time, which could yield more accurate results.

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