

# Measuring Immunoglobulin titer among health care workers after hepatitis B vaccination – A cross sectional study in Kuwait

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## Abstract

**Background:** Hepatitis B viral infection is a major occupational risk hazard among health care workers (HCWs) worldwide. Fortunately, this infection is preventable by vaccine is a, and it is included in the routine immunization program in Kuwait. Measuring anti-HBs antibodies that developed after the vaccine ensures adequate seroconversion rates.

**Methods:** a cross-sectional study among 556 randomly selected HCWs in Farwaniyah health area who met the criteria for completion of 3 doses of the vaccine. After taking consent from the participants, the blood samples were collected and antibody titers were measured by ELISA test. The data was entered and analyzed by SPSS with different categorical variables.

**Discussion:** The results concluded that among the 556 participants, 375 (67.4%) had antibody titer levels above 100 mIU/ml and were hyper-responsive. There was no significant difference between male and female participants; however, age groups between 18-40 and receiving the vaccine within the last 5 years are associated with protective levels. Nursing compared to other health personnel were found to have higher serum titer levels.

**Conclusion:** 67.4% of HCWs in our study responded adequately to the vaccine, with antibody titer levels above 100 mIU/ml. post-vaccination immunity rates in Kuwait is similar to other studies globally. Serum antibody titer levels and an important indicator for vaccine immunogenicity among HCWs and should be considered as a routine testing for all healthcare workers post-vaccination.

**Keywords:** hepatitis b virus; hepatitis b vaccine; healthcare workers; anti-hbs

## Introduction

Hepatitis B virus (HBV) is a highly infectious disease affecting the liver causing life-threatening acute and chronic hepatitis. This viral infection is a major public health burden globally. According to the World Health Organization (WHO) in 2019, 296 million people are chronically infected with HBV worldwide, with 60 million people being in the Eastern Mediterranean Region [1]. In 2019, it was estimated that HBV is responsible for 820,000 deaths worldwide [1].

HBV is transmitted parentally by blood and blood products making it a significant occupational risk for healthcare workers (HCW). Studies showed that HCWs who were injured from HBV contaminated needles with both hepatitis B surface antigen (HBsAg) and HBeAg positive, have a 37%-62% risk of developing serologic evidence of HBV infection [2]. Another study reveals that around 66 000 health care workers acquire HBV infection annually as a result of occupation associated sharps injury, which attributes to an incidence of 5.9% [3].

Due to an increased risk of HBV transmission in HCW compared to the general population [4], the role of vaccination becomes crucial to limit the spread of the disease and protect HCWs. Completion of 3 doses of the HBV vaccine in providing immunity against HBV infection has been demonstrated [5]. The efficacy of the vaccine in terms of protection is measure by the levels of anti-HBs. The centers for disease control and prevention (CDC) reports that seroprotection against HBV is achieved by having anti-HBs levels of  $\geq 10$  mIU/ml [6]. In addition, the hepatitis B vaccination greenbook states that an individual with a titer above 10 mIU/L is considered protected; however, for healthcare and laboratory worker, preferable levels are above 100 mIU/ml [7]. According to the greenbook, having this level ensures that a further dose of vaccine and further titer testing are not required. Consequently, it is recommended to enforce the HBV vaccine among HCWs and measure the levels of antibodies to ensure adequate protection [8].

Our study aims to measure the anti-HBs titers of healthcare workers in Farwaniyah Health District in Kuwait after the completion of 3 doses of the HBV vaccine, therefore providing an insight to the effectiveness of the vaccine in providing immunity to HCWs.

## Methods

### Study design and population

This is a cross-sectional study conducted in Farwaniyah health district area of Kuwait during the time between May to July 2023. Using the Andrew Fisher formula, with a 95% confidence level, a standard deviation of 0.5, and 5% margin of error, a sample size best representing Farwaniyah health population will be at least 385. We collected 556 participants from different departments including physicians, nurses, and laboratory technicians, chosen by simple random sampling. The inclusion criteria for our study population consist of completion of 3 doses of hepatitis B vaccine (Engerix-B recombinant vaccine). Other demographic data were collected from the participants' records available in our public health department. After consent was taken from the participants, blood samples were collected and sent to the microbiology laboratory of the public health department. Measurement of the titers of HbsAg antibodies was done using 4th generation ELISA.

### Data analysis

Our study participants were divided based on different categorical variables including gender, age, specialty, and the time since receiving their last dose. These variables were plotted against the anti-HBs titers. We considered the cut-off level to be 100 mIU/ml for healthcare workers as positive response. The statistical analysis was done using the SPSS 20 software, and both Chi square-test and Fisher's exact test were used to assess the difference in the categorical variables. The p values of <0.05 is considered to be statistically significant.

### Ethical consideration

The study was submitted and approved by the standing committee for coordination of health and medical research department of Kuwait's Ministry of Health, as well as the Director of Farwaniyah Health Area. Consent was obtained from all participants prior to blood collection.

### Results

Our study population consisted of 556 participants meeting the inclusion criteria. Of the total number of participants, 304 (54.7%) were female and 252 (45.3%) were male (Table I). The participants were divided based on their age into two groups. Slightly more than half (52.9%) were between the ages 18-40 and the rest were > 40 years old. The majority of the group were nursing staff (70.5%) compared to physicians (19.7%) and technicians (9.7%). A high proportion (61.2%) received their last dose within the last 5 years.

variables	Number	Frequency
Gender		
male	252	45.3%
female	304	54.7%
Age (years)		
18-40	294	52.9%
>40	262	48.1%
Specialty		
physician	110	19.7%
Nurse	392	70.5%
technician	54	9.7%
Year of receiving vaccine		
≤5 years	340	61.2%
>5 years	216	38.8%
<b>Total number</b>	<b>556</b>	<b>100%</b>

**Table 1: Characteristics of study participants (n = 556).**

Overall, 375 (67.4%) of all HCWs developed a sufficient anti-HBs titer level of  $\geq 100$  mIU/ml, while 181 (32.6%) had levels below 100 mIU/ml (Table II).

After assessing 4 different categorical variables with having protective anti-HBs titer levels, gender was the only category not significantly associated with the outcome (p value =0.103). Ages between 18-40 and receiving the vaccine within the last 5 years are both significant with p values of 0.007 and 0.00001, respectively. Moreover, immunity against HBV is significantly higher in nurses compared to doctors and technicians with a p value of 0.007 (Table II).

variables	<100 mIU/mL n (%)	$\geq 100$ mIU/mL n (%)	X <sup>2</sup>	P-value
<b>Total participants</b>	<b>181 (32.6%)</b>	<b>375 (67.4%)</b>		
Gender				
male	91 (36.1)	161 (63.9%)	2.656	0.103
female	90 (29.6)	214 (70.4%)		
Age (years)				
18-40	79 (26.9%)	215 (73.1%)	9.178	0.002*
>40	102 (38.9%)	160 (61.1%)		
Specialty				
physician	47 (42.7%)	63 (52.3%)	9.665	0.007*
Nurse	112 (28.6%)	280 (71.4%)		
technician	22 (4.7%)	32 (59.3%)		
Time since receiving last dose				
≤5 years	0 (0%)	340 (100%)		< 0.00001**
>5 years	181 (83.8%)	35 (16.2%)		

1 Statistically significant difference (p ≤ 0.05)

2 Fisher exact test is significant at p ≤ 0.05.

**Table 2: Association of different categorical variables with anti-HBs concentrations**

## Discussion

HBV is a serious recognized occupational risk among HCWs worldwide. Although Kuwait has a comprehensive and vigilant HBV vaccination program for all the population including healthcare workers, it is imperative to assess the immunogenicity of the vaccine in order to ensure an adequate and protective response for those with increased exposure. In our study, we assessed 556 HCWs in Farwaniyah health area aged between 18-70 years and measured blood Anti-HBs antibodies levels and deemed them to be protective if levels were above 100 mIU/ml.

The overall percentage of seroprotection was 67.4% which is comparable to findings in a study in Bulgaria and another in Sri Lanka and India that showed 62.7%, 66.2%, and 76.5%, respectively [9-11]. According to our study, 32.2% of the participants had antibody titers below 100 mIU/ml even after receiving 3 doses of the vaccines which in term necessitates providing an additional dose of the vaccine if antibody levels were found to be between 10-100 mIU/ml, or repeating the vaccine course for those found to be non-responders (<10 mIU/ml) as per UK green book guidelines [7].

Our study found a statistically significant difference between age groups below and more than 40 years, with the latter showing lower titer levels. This is also confirmed in a systematic review done in 2016 by Yang et al that assessed different factors influencing HBV vaccine response and found lower response in older adults aged  $\geq 40$  [12]. This might be due to the fact that older participants may have received their vaccine at an earlier time period, which may in turn affect the titer levels as shown in certain studies [10,13]. As demonstrated in our study, titer levels decline with passing time since receiving the last dose of vaccine. Moreover, Gender does not appear to affect the immunogenicity of the vaccine as it was demonstrated in other published papers [10,14]. Interestingly, among the three occupational categories, nurses were found to have significantly higher titers levels compared to doctors and technicians. This might be explained by the fact that the nursing staff are more cautious about their vaccination schedules and boosters as they are more exposed to needle-stick injuries compare to other HCWs [15].

## Limitations and recommendations

Some limitations were faced during our study. Certain factors, such as vaccination schedule and receiving booster doses, were not obtained. Their relationship to the outcome should be explored. In addition, those who have anti-HBs titers below 100 mIU/ml should be further tested to establish whether they are hypo-responders (antibody level between 10-100 mIU/ml) or non-responders (antibody level below 10mIU/ml) and act accordingly.

Our study encourages enforcing a public health program in Kuwait to screen HCWs for evidence of immunity post immunization. Once HCWs are documented to be hyper-responsive, further primary doses and retesting is not necessary [8], and this in turn relieves the economic burden on the ministry of health.

## Conclusion

Among HCWs vaccinated against HBV in Farwaniyah area of Kuwait, 67.4% were responders of the vaccine. Those in younger age groups (< 40 years), and those who receive the vaccine with in the last 5 years, are more likely to be responders. Between the different health professions in the hospital, nurses were found to have higher seroconversion rates. Lastly, post-vaccination testing is necessary for all HCWs to ensure their safety against this occupational exposure.

## List of abbreviations:

HBV	hepatitis B virus
WHO	World Health Organization
HCW	health care worker
HBsAg	hepatitis B surface antigen
CDC	centers for disease control and prevention

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