



Assessment of anti-Hepatitis B surface antibody titers in Hepatitis B vaccinated healthcare workers in Diyala province, Iraq

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Article Info

Article history:

Received 05, 08, 2025
Revised 06, 19, 2025
Accepted 08, 05, 2025
Published 10, 30, 2026

Keywords:

Hepatitis B virus vaccine,
anti-HBs Ab,
HBV infection
Health care workers.

ABSTRACT

Hepatitis B vaccine is one of the safest and most effective vaccines and has been incorporated into national immunization programs worldwide. This study aimed to determine the response rate and anti-HBs antibody titers among healthcare workers (HCWs) immunized with HB vaccine in Diyala. A cross-sectional study was conducted in Diyala Province from June 2024 to June 2025. A total of 360 HCWs of both sexes were included to evaluate the efficacy of the HB vaccination schedule. All participants had received the recommended three doses of HB vaccine. They were recruited from several formations of the Diyala Health Department. Data were collected using a pre-designed questionnaire covering sociodemographic characteristics, vaccination status, and risk factors. Serum samples were tested for anti-HBs antibody titers using ELISA. Statistical analysis was performed using SPSS version 23, with $P < 0.05$ considered statistically significant. The results showed that 316 (87.8%) HCWs were anti-HBs positive (titer >10 mIU/ml), while 44 (12.2%) were negative (≤ 10 mIU/ml). Nine participants (2.5%) were non-responders with zero anti-HBs antibodies. Age 20–29 years ($P=0.006$) and laboratory workers ($P=0.010$) were significantly associated with antibody positivity. Females showed slightly higher positivity than males (88.0% vs. 87.5%, $P=0.880$). Antibody positivity increased from 89.6% among those receiving three doses to 90.5% after four doses and 100% after five doses. High anti-HBs titers were significantly associated with antibody positivity ($P=0.0001$). The study concluded that the national HB vaccination schedule provides a high protection rate among HCWs. Younger age, vaccination at birth, shorter duration since the last dose, and laboratory profession were associated with higher protection.

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1. INTRODUCTION

Hepatitis B is still a major worldwide public health problem. Globally, 296 million people were estimated to be chronic carriers of hepatitis B virus (HBV), with approximately 820,000 deaths per year for complications mainly due to HBV-related cirrhosis and hepatocellular carcinoma (HCC) [1]. Since the early 1990s, the World Health Organization (WHO) has recommended universal vaccination of all infants against HBV, with a minimum of three doses of HB vaccine administered at least four weeks apart [2]. In Iraq, the HB recombinant vaccine was introduced in 1994, including the HCWs as one of the highest risk groups. Hepatitis B vaccine is recommended for all infants (universal vaccination) and children who did not receive HB vaccine during infancy. For adults, it is generally recommended for those who are at increased risk for infection, including all medical, dental, laboratory, and other healthcare staff of hospitals, intimate contacts, or family members of HBV carriers, at-risk patients (Chronic kidney disease with hemodialysis, thalassemia, co-infection of HCV or

HIV), and special groups such as homosexual males, commercial sexual workers, users of illicit drugs [3]. Theoretically, anyone who is susceptible to HBV (negative for HBsAg, anti-HBs, and anti-HBc) may receive the vaccination except for those who have a contradiction [4]. A known history of anaphylaxis or serious adverse events after first injection of HB vaccine is a contraindication for further vaccination. It should also be cautious to vaccinate in individuals with history of allergic to yeast. Additionally, HB vaccination should be delayed in an individual with an acute or febrile disease. HB vaccine does not have additional side effects in pregnant women and can be used during any trimester of pregnancy [5].

Hepatitis B virus is acquired through three main routes; perinatal (vertically), from infected mothers to their newborns; sexually including homosexual and heterosexual; and parenterally (horizontally) via infected blood, blood deprivities and other body fluids, as well as body piercing instruments, tattoos, and injecting-drug use [6]. Admittedly, healthcare workers (HCWs) are at risk for exposure to HBV from infected patients and, if infected, are similarly at risk of transmitting HBV to patients. The transmission risk of viral hepatitis among HCWs is of great concern, as the risk of acquiring HBV by HCWs is four times greater than that of the general population [7]. HCWs are usually infected by HBV via occupational exposure to blood and bodily fluids [8]. In developing countries, 40–60% of HBV infections in HCWs were attributed to professional hazards [9]. The pooled seroprevalences of HBsAg, HBeAg, and acute HBV infection among HCWs were 2.3%, 0.2%, and 5.3%, respectively. The pooled seroprevalences of total immunity against HBV and immunity acquired by natural HBV infection in HCWs were 56.6% and 9.2% respectively. HBV infection was more prevalent in HCWs in low-income countries [10]. In Iraq, HCWs were found as one of prime highly risk group for HBV carriers beside the hemophilia and thalassemia groups [11, 12, 13].

Accordingly, The WHO recommends that HCWs should be vaccinated as per their countries' vaccination schedule and consideration be given as appropriate to vaccinate against the outbreak-prone vaccine preventable diseases [14]. The prime of these diseases is the HB infection. Basically, the highest immunization rates against HBV in HCWs were recorded in urban areas and in high-income countries including Europe, the Eastern Mediterranean and the Western Pacific [10]. In European countries the physicians had consistently higher vaccination rates (79%) than nurses (62%), concluding that vaccine hesitancy among HCWs is impacted by healthcare roles, vaccine types, and regional disparities [15]. Moreover, Gender, occupation, and years of education were significant correlates of receiving the required doses of HB vaccine among HCWs [16].

The HB vaccination coverage and the rate of seroprotection among HCWs were varied over different studies. In Ghana, the seroprotection rate was 91.3 % and 8.7 % had antibody titers below 10mIU/mL and were not seroprotected [17]. In Somalia, only 16.4% of HCWs were fully vaccinated and the main reasons for low coverage rate are the unavailability of the vaccine (42%), high cost (28.7%), lack of time (20.7%), and fear of side effects (7.5%). However, 69.7% of HCWs had good knowledge about HBV infection [18]. In Egypt, 81.7% of HCWs were fully vaccinated, 10.2% refused the vaccine, and vaccination rate was highest (88.1%) among nurses. The overall anti-HBs positivity of 97% was observed [19].

Methods:

Study Subjects:

This is a cross-sectional study conducted in Diyala province-Iraq for the period between Jun 2024 to Jun 2025. A total of 360 HCWs of both sexes were included to evaluate the efficacy of HB vaccination schedule. Basically, all participants were received the recommended 3 doses of HB recombinant DNA vaccine (SERUM of INSTITUTE OF INDIA) at a schedule of (0,1,6) months at the time of employment in health sector. Each dose (1 milliliter) contains 20 mcg purified HBs Ag administered intramuscularly (WHO, 2016). These HCWs were allocated from Baquba Teaching Hospital, Al-Batool Teaching Hospital for Maternity and Children, Baladruz General Hospital, Al-Khalis General Hospital as well as Primary Healthcare Centers (PHCCs) including Al-Jededah, Al-Huyash, Al-Mustafa PHCCs. The mean age $\pm$ SD of HCWs was 29.9 ± 7.1 years with an age range of 22-55 years. Females HCWs were 192 (53.3%) with a slightly higher than males 168 (46.7%). A simple questionnaire form was pre-designed for this study and filled by each participant by short personal interview. It documents sociodemographic information as well as vaccination details. Human privacy was respected by obtaining a verbal consent from each participant.

Sample collection and detection of anti-HBs Abs status and protection titer:

Venous blood samples were collected aseptically; sera were separated and subjected for the detection of anti-HBs antibody titer using enzyme-linked immunosorbant assays (DiaPro, Italy). According to the WHO criteria, HBV vaccinees were considered positive, only if they had ≥ 10.0 mIU of anti-HBs Ab/mL of their sera. A reconstructed questionnaire form was prepared including information of sociodemographic (age, gender and profession), vaccination status, and some risk factors (Jaundice, Surgical intervention, Blood transfusion, Hospitalization and Chronic diseases).

Statistical analysis:

The collected data were coded, entered, presented, and analyzed by computer using the available data base software program statistical package of IBM SPSS-29 (IBM Statistical Packages for Social Sciences- version 29, Chicago, IL, USA). The significance of different percentages (qualitative data) were tested using Pearson Chi-square test (χ^2 -test) with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal or less than 0.05 [20].

4. Results

1. Socio-demographic features:

Results in table 1 showed the distribution of HCWs included in this study according to age, gender and profession. Regarding the age categories, the 20-29 years old HCWs forming the bulk of the study population (62.8%) followed by those 30-39 years forming 26.1% and the least was those with 50-59 years constituting only 3.3%. The mean age $\pm$ SD of study HCWs was 29.9 ± 7.1 years with an age range of 22-55 years.

Concerning the gender, the results found that the females HCWs were 192 (53.3%) with a slightly higher than males 168 (46.7%). The results also found that the laboratory HCWs 183 (50.8%) forming the highest rate of participant profession followed by nurses 112(31.1%) and then administrative HCWs forming 40(11.1), physicians were 13 (3.6%), pharmacists were 9(2.5%) and dentist were 3 (0.8%).

Table 1. Distribution of study group according to age, gender, residency and profession.

Variables		No.	%
Age (Ys)	20--29	226	62.8
	30---39	94	26.1
	40---49	28	7.8
	50--59	12	3.3
Mean age $\pm$ SD (Range)		29.9 $\pm$ 7.1 (22-55)	
Gender	Male	168	46.7
	Female	192	53.3
Profession	Physician	13	3.6
	Dentist	3	0.8
	Pharmacist	9	2.5
	Nurse	112	31.1
	Laboratory worker	183	50.8
	Administrative worker	40	11.1

2. HB vaccination details:

Results in table 2 revealed that the majority of included HCWs 265 (73.6%) were vaccinated at birth, while the remaining 95 (26.4%) were not vaccinated. However, all the included HCWs 360 (100%) were vaccinated at employment in health sector. Regarding the number of vaccine doses administered, the majority of HCWs 221 (61.4) were received 3 doses, and that 21(5.8%) and 5 (1.4%) were received 4 and 5 doses respectively. The results also found that 282 (78.3%) were regularly received their doses versus 78 (21.7%) who received their doses irregularly.

Concerning the duration of time since last vaccine dose, the results recognize three categories; those with 1-4 years duration constituting the bulk of HCWs 257 (71.4%), those with 5-9 years duration constituting 75 (20.8%), and lastly those with 10-15 years duration constituting 28(7.8%). The Mean duration $\pm$ SD was 3.6 ± 3.3 years with a range of 1-15 years.

Table 2. Distribution of study HCWs according to vaccination status, vaccination schedule, number of doses and duration since last dose.

Variables		No.	%
Vaccination at birth	Yes	265	73.6
	Not	95	26.4
Vaccination at employment	Yes	360	100.0
	Not	-	-
Number of vaccine doses	1	44	12.2
	2	69	19.2
	3	221	61.4
	4	21	5.8
	5	5	1.4
Schedule of vaccination	Regular	282	78.3
	Not regular	78	21.7
Duration since vaccination (Ys)	1-4	257	71.4
	5---9	75	20.8
	10-15	28	7.8
Mean duration $\pm$ SD (Range) Ys		3.6 $\pm$ 3.3 (1-15) Ys	

3. Associated risk factors:

As a past history of exposure of HCWs to certain risk factors, the results found that 12 (3.3%) of HCWs had past history of jaundice, 106 (29.4%) had got Surgical intervention, 16 (4.4%) were received blood transfusion, 65 (18.1%) had hospital admission and 20 (5.6%) complaining chronic diseases. Data were shown in table 3.

Table 3. Distribution of study HCWs according to certain risk factors.

Past history of		No.	%
Jaundice	Yes	12	3.3
	No	348	96.7
Surgical intervention	Yes	106	29.4
	No	254	70.6
Blood transfusion	Yes	16	4.4
	No	244	95.6
Hospitalization	Yes	65	18.1
	No	295	81.9
Chronic diseases	Yes	20	5.6
	No	340	94.6

4. Anti-HBs Abs status and protection titer results:

Results in table 4 showed the distribution of anti-HBs Ab status among the study HCWs using the ELISA technique. Regarding the anti-HBs Ab positivity, the results showed that 316(87.8%) were positive versus 44(12.2%) were negative. On the other hand, As the WHO recommendation 316 (87.8%) (Those with HBs Ab titer >10 mIU/ml) were protective against HBV infection and 35 (9.7%) (Those with HBs Ab titer ≤ 10 mIU/ml) were not protective, while 9 (2.5%) were non-responder (those with 0 mIU/ml HBs Ab titer).

Table 4. Distribution of HbsAb among HCWs.

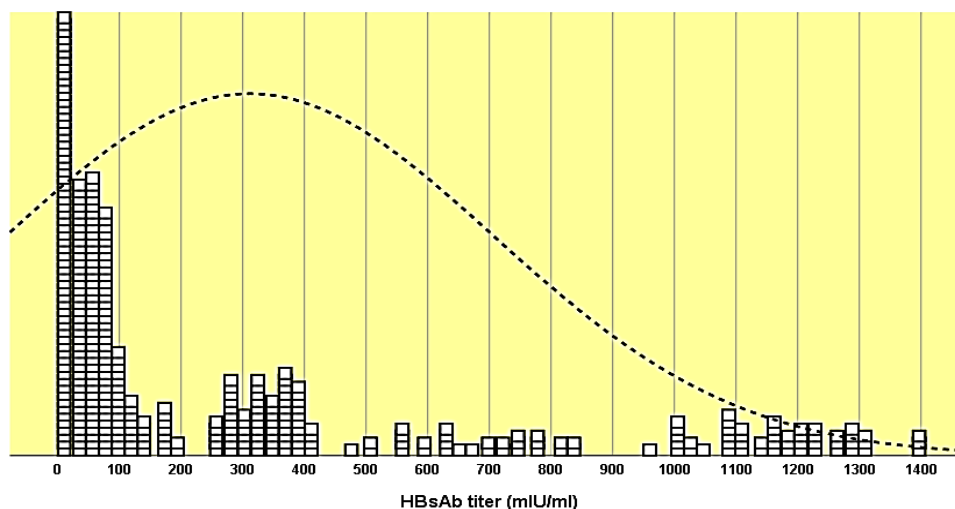
Variables		No.	%
Anti-HBs Ab status	Positive	316	87.8
	Negative	44	12.2
Anti-HBs Ab protection titer	Protective (>10 mIU/ml)	316	87.8
	Not protective (≤ 10 mIU/ml)	35	9.7
	Non-responder (0 mIU/ml)	9	2.5

5. Anti-HBs Ab titer:

Results in table 5 and figure 1 found that the overall mean $\pm$ SD of anti-HBs Ab titer in HCWs included in this study was 311.06 ± 395.9 mIU/ml with a range extended from zero mIU/ml to 1403.93 mIU/ml. the table also showed the 0.5th. To 99th. Percentiles of titer, so the 0.5th. Percentile was 5.486 mIU/ml and the 50th. (Median) percentile was 90.05 mIU/ml, while the 99th. Percentile was 1316.02 mIU/ml.

Table 5. The mean, range and percentiles of anti-HBs Ab titer in HCWs.

Variables		Titer
Mean $\pm$ SD		311.06 $\pm$ 395.9
Standard Error of Mean		20.866
Mode		0
Range		(0-1403.93)
Percentile	05 th	5.486
	25 th	38.086
	50 th (Median)	90.053
	75 th	385.407
	95 th	1209.922
	99 th	1316.029

**Figure 1.** Bar diagram representing the anti-HBs Ab titer indices in HCWs.

6. Association of anti-HBs Ab status with HBs Ab protection status:

Data representing the association between the anti-HBs Ab positivity rate and HBs Ab protection titer were shown in table 6. It was found that 313 (99.1%) of those HCWs who were positive for anti-HBs Ab had protected levels of anti-HBs Ab and 3(8.6%) of HBs Ab positive participants were non-protected and all 9(100%) of those HBs Ab negative were non-responders, the difference was statistically significant ($P = 0.0001$).

Table 6. Association of anti-HBs Ab status with HBs Ab protection status among HCs.

Variable		Anti-HBs Ab status				P value
		Positive		Negative		
		No.	%	No.	%	
HBs Ab protection titer	Protective	316	100.0	-	-	0.0001*
	Not protective	6	15.7	32	84.2	
	Non-responder	-	-	9	100.0	

*Significant difference between percentages using Pearson Chi-square test (χ^2 -test) at 0.05 level.

7. Association of anti-HBs Ab titer with sociodemographic features:

Data showing the association of between the anti-HBs Ab and the age categories were presented in table 7. the result revealed that the 20-29 years age category had significantly higher anti-HBs Ab titer (350.874 ± 418.147 mIU/ml) compared to other age categories ($P=0.029$).

Regarding the gender, the female HCWs had insignificantly higher anti-HBs Ab titer versus that of male (341.094 ± 406.201 Vs 276.736 ± 382.119 mIU/ml), ($P= 0.124$). Additionally, the results found that physicians had obviously higher titer of anti-HBs Ab (526.202 ± 525.074 mIU/ml) compared to other HCW categories; However, the difference was failed to reach the levels of statistical significant ($P=0.424$).

Table 7. Association of anti-HBs Ab titer with sociodemographic features among HCs.

Variable		Anti-HBs Ab titer (mIU/ml)		P value
		No.	Mean $\pm$ SD	
Age (Ys)	20--29	226	350.874 $\pm$ 418.147	0.029*
	30---39	94	279.666 $\pm$ 365.840	
	40---49	28	139.291 $\pm$ 274.918	
	50--59	12	207.963 $\pm$ 307.126	
Gender	Male	168	276.736 $\pm$ 382.119	0.124
	Female	192	341.094 $\pm$ 406.201	
Profession	Physician	13	526.202 $\pm$ 525.074	0.424
	Dentist	3	168.418 $\pm$ 164.051	
	Pharmacist	9	341.571 $\pm$ 407.854	
	Nurse	112	304.001 $\pm$ 405.191	
	Lab. workers	183	311.772 $\pm$ 390.691	
	Adm. worker.	40	261.485 $\pm$ 350.751	

*Significant difference among more than two independent means using ANOVA-test at 0.05 level.

8. Association of anti-HBs Ab titer with vaccination details:

Basically, all HCW participants included in this study were vaccinated with HB vaccine at the employment time. The implementation of universal HB vaccination was started in Iraq at 1994. Therefore, those born in 1994 and thereafter supposed to be vaccinated at birth too. Results in table 8 found that HCWs who were previously vaccinated at birth had significantly higher anti-HBs Ab titer (342.338 $\pm$ 409.643 mIU/ml) compared to those who not vaccinated at birth (223.813 $\pm$ 341.879 mIU/ml), (P=0.012). Referring to the number of vaccine doses, the results revealed that those HCWs received 4 vaccine doses (three basic doses and one booster dose) had significantly higher anti-HBs Ab titer (735.522 $\pm$ 566.941 mIU/ml) compared to other categories (P=0.0001). Regarding the schedule of vaccine administration, the result found that those received their vaccine doses regularly had higher anti-HBs Ab titer (328.915 $\pm$ 403.309 mIU/ml) compared to those received their vaccine irregularly (246.510 $\pm$ 363.045 mIU/ml); however, the difference was statistically insignificant (P=0.104). concerning the time duration elapse since last vaccine dose, it was found that those HCWs who vaccinated before 1-4 years had significantly higher HBs Ab titer (345.540 $\pm$ 410.789 mIU/ml) compared to those who vaccinated before 5-9 years (240.754 $\pm$ 347.961 mIU/ml) and those who were vaccinated before 10-15 years (182.913 $\pm$ 331.965 mIU/ml), (P=0.026).

Table 8. Association of anti-HBs Ab titer with vaccination details among HCs.

Variable		Anti-HBs Ab titer (mIU/ml)		P value
		No.	Mean $\pm$ SD	
Vaccination at birth	Yes	265	342.338 $\pm$ 409.643	0.012**
	Not	95	223.813 $\pm$ 341.879	
Vaccination at employment	Yes	360	311.060 $\pm$ 395.907	-
	Not	-	-	
No. of vaccine doses	1	44	221.381 $\pm$ 326.130	0.0001*
	2	69	247.732 $\pm$ 361.502	
	3	221	302.811 $\pm$ 373.455	
	4	21	735.522 $\pm$ 566.941	
	5	5	556.071 $\pm$ 492.367	
Schedule of vaccination	Regular	282	328.915 $\pm$ 403.309	0.104
	Not regular	78	246.510 $\pm$ 363.045	
Duration (years)	1-4	257	345.540 $\pm$ 410.789	0.026*
	5---9	75	240.754 $\pm$ 347.961	
	10-15	28	182.913 $\pm$ 331.965	

. **Significant difference between two independent means using Students-t-test at 0.05 level.

*Significant difference among more than two independent means using ANOVA-test at 0.05 level.

9. Association of anti-HBs Ab titer with risk factors:

Generally, none of these risk factors had considerable effect on the titer of anti-HBs Ab among HCW participants. So, HCWs who were reported previous history of jaundice had insignificantly higher anti-HBs Ab titer (338.364 $\pm$ 451.655 *Vs* 310.119 $\pm$ 394.550 mIU/ml), (P=0.808). Similarly, HCWs who had previous surgical intervention had insignificantly higher titer of anti-HBs Ab compared to their counterpart (280.354 $\pm$ 388.360 *Vs* 323.875 $\pm$ 399.072 mIU/ml), (P=0.342). Likewise, those revied blood transfusion were

found to had insignificantly higher titer of anti-HBs Ab compared to their counterpart (373.528 ± 520.703 Vs 308.155 ± 389.880 mIU/ml).

The results also found that HCWs with no history of hospitalization had insignificantly higher titer of anti-HBs Ab compared to their counterparts (316.424 ± 392.386 Vs 286.720 ± 413.771 mIU/ml) ($P=0.585$). Also, HCWs complaining no chronic diseases had insignificantly higher titer of anti-HBs Ab compared to those with chronic diseases (317.972 ± 399.689 Vs 193.562 ± 309.713 mIU/ml), ($P=0.172$). All data were shown in table 9.

Table 9. Association of anti-HBs Ab titer with risk factors among HCWs.

Variables		HBs Ab titer (mIU/ml)		P value
		No.	Mean $\pm$ SD	
History of jaundice	Yes	12	338.364 ± 451.655	0.808
	Not	348	310.119 ± 394.550	
History of surgical intervention	Yes	106	280.354 ± 388.360	0.342
	Not	254	323.875 ± 399.072	
History of blood transfusion	Yes	16	373.528 ± 520.703	0.519
	Not	344	308.155 ± 389.880	
History of hospitalization	Yes	65	286.720 ± 413.771	0.585
	Not	295	316.424 ± 392.386	
History of chronic diseases	Yes	20	193.562 ± 309.713	0.172
	Not	340	317.972 ± 399.689	

Discussion:

Hepatitis B virus represents a worldwide public health problem, causing major morbidity and mortality. Affordable, safe, and effective, hepatitis B vaccines are the best tools we have to control and prevent hepatitis B ⁽²⁾. Although the 20-29 years is forming the highest rate in this study compared to other age categories; however, generally the age range 22-55 years included is covering the most prevalent ages of the HCWs who are already in local health services. Probably because those less than 20 years are not yet employed, while older than 55 years are near the retardation age.

The slightly higher rate of female HCWs over that of males is logical, as health services hiring more females than males. Furthermore, females are generally preferring health sector for employment rather than other working sectors.

Regarding the sample number of HCWs profession included are non-homogenous, as the highest rate is belonged to laboratory workers and nurses (81.9%). On the other side, the participation of physicians, dentists and pharmacists is unfortunately weak (6.9%). This is most probably due to that the participation in this study is optional and nothing obligate employees to take part. Anyhow, the laboratory workers and nurses are playing a big role in transmitting blood transmitted viruses, particularly the HBV, as they directly dealing with the blood and its derivatives as well as other body fluids which are undoubtedly highly infectious ^(8,9).

The HBV genetically engineered vaccine was introduced in the Iraqi at 1994, as universal vaccination for newly born and all other high-risk groups in the community including the HCWs in an obligatory manner. Therefore, it was unsurprisingly found that 73.6% of HCWs included in this study were previously received HBV vaccine at birth because they are less than 31 years old. While the remaining 26.4% were not vaccinated at birth because they were boned before 1994. What is more importantly is that all HCWs included in the current study were vaccinated at employment in health sector. Therefore, it is easily interpreted that the 73.6% who were vaccinated at birth were received another set of HBV vaccine at the time of employment in the health services, that is to say, they are vaccinated twice, and scientifically they should be double protected.

Admittedly, there was a global consensus of the critical role of HCWs in transmitting HBV particularly in intermediate and high endemic countries ⁽¹³⁾. Since it was found that the global pooled seroprevalences of HBsAg, HBeAg, and acute HBV infection among HCWs were 2.3%, 0.2%, and 5.3%, respectively particularly in African countries ⁽¹⁰⁾. The transmission risk of viral hepatitis among HCWs is of great concern worldwide, as the risk of acquiring HBV by HCWs is four times greater than that of the general population ⁽⁷⁾. As HCWs are at risk for acquiring HBV from infected patients, they are similarly at risk of transmitting HBV to patients or other HCWs. They are usually infected by HBV via occupational exposure to blood and other bodily fluids ⁽⁸⁾. In developing countries, 40–60% of HBV infections in HCWs were attributed

to professional hazards ⁽⁹⁾. They are also vulnerable to contaminate sharp injuries which constitute a major source of HBV infection, with an estimated 66,000 cases and 261 deaths annually in developing countries [21]. However; despite that, about 80% of HCWs remain unimmunized (against HB) in many parts of the world [22].

For these reasons and since there were worldwide certainties that HB vaccine is the most effective strategy to control HBV infection and disease [16, 23]. So, the core theme is that successful coverage and vaccination of HCWs will end one of the important HBV infection tributaries and thus reducing nosocomial and community transmission of HBV [4].

These risk factors were considered as their presence may increase the infection rate by HBV [6]. Of these 3.3% of included HCWs had past history of jaundice which is denote the increase in bilirubin pigment in the blood, and clinically presented as yellow eye sclera, deep yellow urine and pale stool as well as yellow skin. Appearance of these clinical signs may indicate hepatitis [24]. Furthermore, 18.1% of included HCWs had hospital admission, 4.4% had received blood transfusion and 29.4% had surgical intervention, these high-risk practices may also increase the probability of getting infection with blood transmitted viruses such as HBV [4]. The presence of chronic diseases had bidirectional impact; from one side, it may increase the susceptibility of HCWs for infection by viruses like HBV as well as other opportunistic pathogens and from other side, it may affect the efficacy of HBV vaccine, since most patients with chronic diseases suffering certain degrees of immune dysfunction [25].

One of the central results in this study is that 87.8% of the participating HCWs were positive for anti-HBs Ab versus 12.2% who were appeared as negative for these antibodies. That is to say, the HBV vaccine efficacy in HCWs was 87.8%. Furthermore, all these anti-HBs Ab positive HCWs (87.8%) had a titer of >10 mIU/ml, therefore, they are protective against HBV infection according to the definition of the WHO ⁽¹⁾. The 12.2% anti-HBs Ab negative HCWs were either non-protective, those forming 9.7% who had a titer of anti-HBs Ab equal or less than 10 mIU/ml, or those non-responders forming 2.5% who had zero titer of anti-HBs Ab. Unfortunately, upon reviewing the scientific literature, no previous study was conducted on the efficacy of HBV vaccine in HCWs in Iraq. However, it was found that among universally vaccinated children 1-14 years old received the three standard vaccine doses at a schedule (0,1,3), the overall anti-HBs Ab positivity rate was 75.66%, with a range of anti-HBs Ab titers (10.1 – 673.4 mIU/ml) [26]. In another study among children 1-10 years received 3 primary vaccine doses, the protective level of anti-HBs Ab was 77.2 % [27].

Globally different studies had yielded different efficacy rates, but basically, the highest immunization rates against HBV in HCWs were recorded in high-income countries including Europe, the Eastern Mediterranean and the Western Pacific [10]. Global studies on HBV in HCWs from 2017 till 2023, found a wide variation on the prevalence of infection ranging from 0.6% in Europe to >8.7% in Africa, almost always in association with very low vaccination rates [28].

Compared to the present study, worldwide similar studies have reported variable efficacy rates. In Egypt, 81.7% of HCWs were completed the 3 doses of the HBV vaccine [19]. In Isfahan-Iran, 23.2% of employers of clinical laboratories were not immune, 62.0% were relatively immune, and 14.8% were highly immune, All participants were negative for HBV infection [29].

Regarding the non-protected and non-responders who constituting 9.7% and 2.5 of the participating HCWs respectively. They failed to mount >10 mIU/ml titer of anti-HBsAb or not at all at the time of testing. Of course, those non-responders remain susceptible to infection with HBV. Factors contributing to the non-response, ranging from epidemiological factors to defective immunological mechanisms and genetic polymorphisms involving antigen-presenting cells, cytokines, and cytokine receptors [30, 31, 32]. Additionally, non-response to the HB vaccine is not only related to vaccinee-associated factors such as age, sex, obesity, and smoking, but may also depend on the nature of the vaccine, dose, and type of adjuvants used [33, 34]. Based on these facts, the present study suggest that low responding or non-responding HCWs should be strictly enforced to administered the first and second booster doses of the vaccine, and if it doesn't work, then to give double dose vaccine 40 µg or 60 µg instead of 20 µg, since the 60 µg HB vaccine was found to be safe and gives rapid seroprotection in adult [35].

The current study two methods to classify the vaccinated HCWs, one was based on the positivity of anti-HBs Ab and the second one was based on the titer of these antibodies in the vaccinated participants.

According to the WHO guidelines, an anti-HBs level of >10 mIU/ml is considered protective against HBV infection [1]. Generally, our study found that the mean $\pm$ SD of the anti-HBs Ab titer among vaccinated HCWs was 311.06 ± 395.9 mIU/ml with a range of 0 -1403.93 mIU/ml. Unfortunately, most similar studies didn't mention the anti-HBs Ab titer and instead classified the vaccinated HCWs as a protective (with >10 mIU/ml), non-protective (with <10 mIU/ml) and non-responders (with zero mIU/ml). However, lower anti-HBs Ab titer (mean $\pm$ SD 36.46 ± 42.3 mIU/ml) was obtained in vaccinated HCWs (mean age $\pm$ SD 32.1 ± 8.7 years) received ≥ 3 doses after 1-2 months postvaccination in Cameroon [36]. In India, HCWs with mean age 27.2 ± 0.56 years had postvaccination antibody titers > 100 mIU/ml in 85.0%, 10-100 mIU/ml in 11.0% and 10 mIU/ml in 3.5% [37].

The current results showed that not all HCWs who were positive for anti-HBs Ab had protected titers of these antibodies (≥ 10 mIU/ml) according to the WHO recommendation [1]. Most of studies conducted to explore the efficacy of HB vaccine used the WHO scoring system [26, 36, 38, 39]. To be more comprehensive, the present study use both qualitative and quantitative scoring approaches. However, the study suggest that in countries like Iraq, where most of HCWs were vaccinated twice; one at infancy and the second at employment, and to achieve fully protected HCWs, the minimum positive HBs Ab titer should be increased such as ≥ 20 mIU/ml. Regarding the association between the anti-HBs Ab positivity and participant age, the results found that there was a significantly higher positivity rate with 20-29 years. Furthermore, this age category also had significantly higher anti-HBs Ab titer compared to other age categories.

Similar result was obtained by Latt *et al.*, (2022) [40] who found that the age 20-29 years had higher anti-HBs Ab positivity. the present result also in agreement with that of Shoaie *et al.*, (2015)[26] who reported that the highest anti-HBs Ab titer (76.63 ± 92.9 mIU/ml) was found among those 20-30 years old and also with that of Thomas *et al.* (2022) [21]who affirmed that age >40 years were independent predictors for poor seroprotection in HCWs. However, the current result is inconsistent with Mwangi *et al.*, (2023) [39] who stated that age was not determinants of immune response after HB vaccination. In another study, 41.4% of the vaccinated HCWs who had anti-HBs Ab titer of ≥ 10 mIU/ml were 26-35 years [41]. In China, 62.3% of HCWs who complete their vaccine doses was 30-39 years old [42]. Admittedly, the discrepancy in results among different studies was attributed to wide range of determinants. However, the outcome of the present study is the most acceptable one, because, undoubtedly, this (20-29) year's age category had fully developed and efficient immune system that able to provoke excellent immune response [43].

Female HCWs were appeared to have slightly higher anti-HBs Ab positivity rate compared to that of male and also had insignificantly higher anti-HBs Ab titer versus that of male. This result is consistent with some other studies [29, 39, 41]. Lower response among male participants was also reported by [44]. Moreover, sex disparity in response to HB vaccine reported that females showed 20% higher vaccination-related antibody titers than males [45]. As it was clearly evident that female HCWs had better response to HB vaccine probably owing to the opposite effects of sex hormone androgen and estrogen. Estrogen activates monocytes to secrete IL-10, which induces IgG and IgM secretion via B-cells in turn, while testosterone damages the production of IgG and IgM from B-lymphocytes, and restrains producing IL-6 from monocytes [44]. Furthermore, the low immune response among males may be attributed to smoking, alcohol and certain genetic factors [39]. In our community, fear of social and health stigma, generally make women more commitment than males, of these is adherence to vaccines accomplishment. Probably, the most astonishing result in table (7), is that the anti-HBs Ab positivity rate in nurses, laboratorians and administrative staff was significantly higher than physicians, dentists and pharmacists. However, the physicians had obviously higher titer of anti-HBs Ab compared to other HCW categories; but the difference was failed to reach the levels of statistical significant. Fewer worldwide studies focused on the association of HCW occupation and response to HB vaccine. Shoaie *et al* (2015) [29] from Iran didn't find a significant difference in the mean $\pm$ SD of anti-HBs Ab among technologist, laboratory technicians and laboratory cleaning staff. Duodu *et al.*, (2022) [16] in their study about the prevalence and socio-demographic factors associated with HB vaccination in 5 developing countries, found that occupational qualification was significantly associated with receiving the required doses of HB vaccine, but the category of the qualification that was protective varied from country to another; nurses and midwives and other professionals, compared to medical doctors, were more likely to receive the required doses of HB vaccine in Afghanistan, while it was the contrary in in Haiti, Malawi, Nepal and Senegal. In India, Sahana *et al.* (2017) [46] found that the HB vaccine coverage among staff nurses, nursing students and medical students were higher

than that of doctors, technicians and housekeeping staff. Thus, nearly all worldwide studies agree that the HB vaccination coverage of physicians and pharmacists is generally low, even the participating numbers of physicians and pharmacists in these studies were less than other HCWs. Thus, the current study recommends rigorous and accurate follow up of unvaccinated, partially vaccinated or non-responder HCWs particularly physicians and pharmacists by obligatory testing them for anti-HBs Ab from time to time, and be considered that as one of the fulfillments for occupational or financial promotion.

Several important results were raised in table (8); logically, this occur because 78.9% of the participating HCWs are younger than 31 years i.e. they born after the implementation of HB vaccine in the Iraqi EPI in 1994. Vaccination of HCWs at the time of employment is important as the rate of subjects who were unprotected after 5 and 10 years after vaccination were 20% and 27%, respectively [46]. Furthermore, a significant decline in anti-HBs antibody titers as duration of post vaccination was increased probably due to wanning immunity by age [37, 44, 47, 48]. Nearly 16% of people vaccinated at the age of <1 year had detectable antibody levels ≥ 10 mIU/ml at 18 years of vaccination, compared to 74% for those vaccinated at age ≥ 1 year [49]. As the importance of HCWs not only due to their high susceptibility to HBV infection but also because they may serve as potential sources of infection during high-risk procedures, and to keep them always fully protective, the HBV vaccination and regular anti-HBs checks mandatory for HCWs is imperative.

Regarding the number of vaccine doses administered, the current study obtained a marvelous results, since the majority (89.6%) of HCWs completed 3 vaccine doses were positive for anti-HBs Ab. The positivity rate was increased to 90.5% in those received additional booster dose and to 100% in those received the second booster dose. Appropriately, results are also found that HCWs received 4 vaccine doses (three basic doses and one booster dose) had significantly higher anti-HBs Ab titer (735.522 ± 566.941 mIU/ml) compared to other categories ($P=0.0001$). The current results were in agreement with those reported by Coppeta *et al.* (2019) [38] reported that primary immunization in childhood is highly effective and provides lasting immunity against HBV infection. It also consistent with the finding that completion of HB vaccination associated with increased positivity rate [42]. The present results totally consistent with the findings confirms that HB vaccination at adolescence may determine a higher long-term persistence of anti-HBs Ab titers ≥ 10 mIU/mL and that booster dose could increase levels of anti-HBsAb over a relatively short period, especially in people who were vaccinated during infancy [50].

The Iraqi vaccination schedule for HCWs is 0, 1, 6, followed by first and second booster doses, each dose contain 20 μ g purified HBsAg. The preset study found that there was insignificant difference in response to HB vaccine between regular versus irregular vaccine administration. Additionally, those received their vaccine doses regularly had higher anti-HBs Ab titer (328.915 ± 403.309 mIU/ml) compared to those received their vaccine irregularly (246.510 ± 363.045 mIU/ml); however, the difference was statistically insignificant ($P=0.104$). Similar result was reported by [44] who found that there was no differences in response to HB vaccine by vaccination schedule. However, another study showed a higher seroconversion rate in individuals with the 0-1-12 schedule [51].

In the light of these facts, the current study encourage continuation and more adherence to the current national vaccination policy for HCWs with 3 basic adult doses (20 μ g) as 0,1,6 schedule with two booster doses (20 μ g) annually. This will surely afford complete protection of nearly all HCWs except non-responders who required special attention. Also importantly, HCWs who work in non-governmental health institutes such as private hospitals, private clinics, and cosmetic clinical centers should also include and followed appropriately. More importantly, non-qualified persons who works in cupping, the newly emerging phenomenon, should also vaccinated and followed up strictly.

Among the included risk factors, the anti-HBs Ab positive HCWs with past history of hospitalization were significantly lower than their counterpart. All other listed risk factors were insignificantly associated with anti-HBs Ab positivity. Furthermore, none of these risk factors had considerable effect on the titer of anti-HBs Ab among HCW participants. Primarily these information were based on self-reporting by HCWs that is to say without medical records. Jaundice is a yellowish or greenish pigmentation of the skin and sclera due to high bilirubin levels. It is typically a sign indicating the presence of underlying diseases involving abnormal heme metabolism, liver dysfunction, or biliary canal obstruction [52]. So, it could be due to a wide range of physiological and pathological conditions including infectious and non-infectious disease, that is to say, it is not specific to viral hepatitis [53]. Unsafe surgical intervention or by non-authorized persons, frequent

hospitalization and blood or blood products transfusion of unknown sources, all these high risk practices may bear risks for the transmission of blood transmitted viruses including HBV. of not, mandatory testing of all Iraqi donated blood pints for HBV, HCV and HIV as well as other infectious agents since 1987. Patients with concomitant chronic diseases usually have a complicated and inconstant status due to diverse pathogenesis. Although some studies reported no association between comorbidity and HBs Ab seroprotection [54]. On the contrary, comorbidity may be a significantly decreasing the efficacy of HB vaccine [43, 55]. Chronic conditions, such as chronic alcoholism, chronic kidney disease, human immunodeficiency virus infection, immune-suppression, T1DM and Celiac disease are characterized by a lower response to HB vaccination [55].

Conclusions:

The study concluded that the compulsory HB national vaccination schedule among HCWs yield high protection rate. Younger age, vaccination at birth, duration since last vaccine dose and laboratorians profession were associated with high protection rate.

Ethical approval:

This study was approved by the scientific committee of the Department of biology-College of Science, University of Diyala under an Issue No. 3193 at 19/8/2024. The study was also approved by the scientific committee of the Directorate of Health in Diyala province under an issue No. 38219 at 17/9/2024.

Source of Funding: This research was funded by the authors themselves.

Conflict of Interest: The author declares no conflict of interest.

References:

- [1] WHO. (2022). Hepatitis B Vaccine and Multiple Sclerosis. (accessed on 9 June 2022). Available online: <https://www.who.int/groups/global-advisory-committee-on-vaccine-safety/topics/hepatitis-b-vaccines/multiple-sclerosis>.
- [2] J. Pattyn, G. Hendrickx, A. Vorsters, and P. Van Damme, "Hepatitis B Vaccines", The Journal of Infectious Diseases, 224 (4), 1S343–S351(2021), DOI: <https://doi.org/10.1093/infdis/jiaa668>.
- [3] World Health Organization, "Hepatitis B vaccines: WHO position paper—July 2017", Weekly epidemiological record, 27, 369-92(2017).
- [4] S. A. Al-Busafi, and A. Alwassief, "Global Perspectives on the Hepatitis B Vaccination: Challenges, Achievements, and the Road to Elimination by 2030", Vaccines (Basel), 12(3), 288(2024), DOI: [10.3390/vaccines12030288](https://doi.org/10.3390/vaccines12030288).
- [5] X. Gong, Q. Fang, J. Zhong, C. Zheng, and Z. Yin, "Adverse event reporting following immunization of hepatitis B vaccine: A 13-year review", Hum. Vaccin Immunother, 20(1), 2411824(2024), DOI: <https://doi.org/10.1080/21645515.2024.2411824>.
- [6] D. A. Asandem, S. P. Segbefia, K. A. Kusi, and J. H. Bonney, "Hepatitis B Virus Infection: A mini review", Viruses, 16(5), 724(2024), DOI: [10.3390/v16050724](https://doi.org/10.3390/v16050724).
- [7] T. A. Abebaw, Z. Aderaw, and B. Gebremichael, "Hepatitis B virus vaccination status and associated factors among health care workers in Shashemene Zonal Town, Shashemene, Ethiopia: a cross-sectional study", BMC Res Notes, 10(1), 1-9(2017), DOI: [10.1186/s13104-017-2582-0](https://doi.org/10.1186/s13104-017-2582-0).
- [8] T. Sekamatte, T. Mukama, S. P. Kibira, R. Ndejjo, J.N. Bukenya, Z. P. Kimoga, "Hepatitis B screening and vaccination status of healthcare providers in Wakiso district, Uganda", PLoS One, 15(7), 1-13(2020), DOI: [10.1371/journal.pone.0235470](https://doi.org/10.1371/journal.pone.0235470).
- [9] D. Kisic-Tepavcevic, M. Kanazir, T. Gazibara, G. Maric, N. Makismovic, G. Loncarevic, "Predictors of hepatitis B vaccination status in healthcare workers in Belgrade, Serbia, December 2015" Eurosurveillance, 22(16), 0-8(2017), DOI: [10.2807/1560-7917.ES.2017.22.16.30515](https://doi.org/10.2807/1560-7917.ES.2017.22.16.30515).
- [10] G. Mahamat, S. Kenmoe, E. W. Akazong, J. T. Ebogo-Belobo, D. S. Mbagi, A. Bowo-Ngandji, "Global prevalence of hepatitis B virus serological markers among healthcare workers: A systematic review and meta-analysis" World J. Hepatol., 13(9), 1190-202(2021), DOI: [10.4254/wjh.v13.i9.1190](https://doi.org/10.4254/wjh.v13.i9.1190).
- [11] A. SH. Hasan, A. R. Omer, and J. I. Al-Mashhadani, "Seroepidemiological study of hepatitis B virus infection among blood donors and risky groups in Diyala", Iraqi J. Commun. Med., 19(1), 14-8(2006).
- [12] M.O. Mohammed, "Prevalence of Hepatitis B virus Infection Among Premarital People in Sulaimani Governorate", Ir. Post graduate. Med. J. 11, suppl., (2012).
- [13] Global Burden of Disease (GBD) (2019), "Hepatitis B Collaborators, Global, regional, and national burden of hepatitis B, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019", Lancet Gastroenterol Hepatol., 7(9), 796-829(2022), DOI: [10.1016/S2468-1253\(22\)00124-8](https://doi.org/10.1016/S2468-1253(22)00124-8).
- [14] WHO, Global Health Sector Strategy on Viral Hepatitis 2016–2021, Towards Ending Viral Hepatitis. World Health Organization; Geneva, Switzerland: 2016. (accessed on 14 April 2022), Available: <https://apps.who.int/iris/handle/10665/246177>.
- [15] M. Kaur, L. Coppeta, and O. F. Olesen, "Vaccine Hesitancy among Healthcare Workers in Europe: A Systematic Review" Vaccines (Basel), 11(11), 1657(2023), DOI: [10.3390/vaccines11111657](https://doi.org/10.3390/vaccines11111657).
- [16] P. A. Duodu, E. Darkwah, P. Agbadi, H. O. Duah, and J. J. Nutor, "Prevalence and geo-clinodemographic factors associated with hepatitis B vaccination among healthcare workers in five developing countries" BMC Infect Dis., 22(1), 599(2022), DOI: <https://doi.org/10.1186/s12879-022-07556-3>.
- [17] E. S. Vivian, D. Armah, and A.W. Delali, "Hepatitis B virus vaccination post serological testing and antibody levels of vaccinated health care workers in Accra", Ghana. Vaccine X., 14, 100294(2023), DOI: <https://doi.org/10.1016/j.jvax.2023.100294>.
- [18] N. A. Hussein, A. M. Ismail, and S. S. Jama, "Assessment of Hepatitis B Vaccination Status and Associated Factors among Healthcare Workers in Bosaso, Puntland, Somalia 2020", Biomed Res Int. 2022, 9074294(2022), DOI: <https://doi.org/10.1155/2022/9074294>.

- [19] M. Elshaer, E. Elsayed, A. H. El-Gilany, N. El-Mashad, and M. Mansour, "Adherence and Effectiveness of HBV Vaccination among Healthcare Workers in Egypt", *Indian J Occup Environ Med.*, 25(2), 91-95(2021), DOI: https://doi.org/10.4103/ijoem.IJOEM_139_20.
- [20] W. Wayne, N. Daniel, and L. Chad, "Biostatistics: A Foundation for Analysis in the Health Sciences", Cross, 11th ed. John Wiley & Sons Inc, USA, 2019, PP: 600-670.
- [21] B. Thomas, A. Mohandas, V. K. Jayadev, and V. Bindu, "Hepatitis B surface antibody levels among health-care personnel vaccinated against hepatitis B in a teaching hospital in South India", *Indian J Community Med*, 47, 262-5(2022), DOI: [10.4103/ijcm.ijcm_600_21](https://doi.org/10.4103/ijcm.ijcm_600_21).
- [22] J. G. Nora, S. Dykki, D. Luke, and E. D. Brian, "Chapter 14 - Health worker registries: managing the health care workforce, Editor(s): Brian E. Dixon, Health Information Exchange (Second Edition), Academic Press, 2023, 329-341(2023).
- [23] D. Razavi-Shearer, I. Gamkrelidze, C. Pan, J. Jia, T. Berg, R. Gray, "Global prevalence, cascade of care, and prophylaxis coverage of hepatitis B in 2022: A modelling study", *Lancet Gastroenterol. Hepatol.*, 8, 879–907(2023), DOI: [https://doi.org/10.1016/s2468-1253\(23\)00197-8](https://doi.org/10.1016/s2468-1253(23)00197-8).
- [24] M. Ocan, F. Acheng, C. Otiike, J. Beinomugisha, D. Katete, and C. Obua, "Antibody levels and protection after Hepatitis B vaccine in adult vaccinated healthcare workers in northern Uganda", *PLoS ONE*, 17(1), e0262126(2022), DOI: <https://doi.org/10.1371/journal.pone.0262126>.
- [25] M. Mironova, and M. G. Ghany, "Hepatitis B Vaccine: Four Decades On", *Vaccines*, 12, 439(2024), DOI: <https://doi.org/10.3390/vaccines12040439>.
- [26] M. M. Mustaf, and A. SH. Hasan, "The efficacy of hepatitis B virus vaccine among children in Baquba-Diyala province", *Iraqi Journal of Community Medicine*, 30 (3 & 4), 176-181(2018).
- [27] F. Alfaleh, S. Alshehri, S. Alansari, M. Aljeffri, Y. Almazrou, A. Shaffi, A. A. Abdo, "Long-term protection of hepatitis B vaccine 18 years after vaccination", *J Infect.*, 57(5), 404-9(2008).
- [28] G. B. Nikolopoulou, I. Tzoutzas, A. Tsakris, and H. C. Maltezou, "Hepatitis B in Healthcare Personnel: An Update on the Global Landscape", *Viruses*, 15(12), 2454(2023), DOI: <https://doi.org/10.3390/v15122454>.
- [29] P. Shoaie, S. Najafi, N. Lotfi, B. Vakili, B. Ataie, M. Yaran, "Seroprevalence of hepatitis B virus infection and hepatitis B surface antibody status among laboratory health care workers in Isfahan, Iran", *Asian J Transfus Sci.*, 9(2), 138-40(2015), DOI: [10.4103/0973-6247.162701](https://doi.org/10.4103/0973-6247.162701).
- [30] L. Pan, W. Zhang, Z. Liang, X. Wu, X. Zhu, J. Li, "Association between polymorphisms of the cytokine and cytokine receptor genes and immune response to hepatitis B vaccination in a Chinese Han population", *J. Med. Virol.*, 84, 26–33(2012), DOI: <https://doi.org/10.1002/jmv.22251>.
- [31] Z. Borzoo, A. Streinu-Cercel, A. Mirshafiey, A. Khamseh, M. K. Mahmoudie, S. S. Navabi, "IL-17 and IL-22 genetic polymorphisms in HBV vaccine non-and low-responders among healthcare workers" *Germs*, 6, 14(2016), DOI: <https://doi.org/10.1159/germs.2016.1084>.
- [32] Z. Rui-jun, Y. Lin-zhu, W. Jia-xin, Z. Tian-jing, L. Yan-di, W. Ting, « The effects of TLR3 up-regulation on Th1/Th2 cytokines in CBMCs of infants with non/hypo response to hepatitis B vaccine", *Chin. J. Disear Control. Prev.*, 24, 711–15(2021).
- [33] S. A. Hudu, S. H. Shinkafi, and S. Umar, "An overview of recombinant vaccine technology, adjuvants and vaccine delivery methods", *Int. J. Pharm. Pharm. Sci.*, 8, 19–24(2016), DOI: <https://dx.doi.org/10.22159/ijpps.2016v8i11.14311>.
- [34] R. P. Medeiros, N. A. Terrault, D. F. Mazo, C. P. Oliveira, J. Dodge, P. M. Zitelli, "Impaired anti-HBV vaccine response in non-cirrhotic chronic HCV is not overcome by double dose regimen: Randomized control trial", *Ann. Hepatol.*, 28, 100891(2023), DOI: <https://doi.org/10.1016/j.aohp.2022.100891>.
- [35] L. Y. Wang, C. F. Chen, T. W. Wu, S. K. Lai, C. C. Chu, and H. H. Lin, "Response to hepatitis B vaccination is co-determined by HLA-DPA1 and-DPB1", *Vaccine*, 37, 6435–6440(2019), DOI: <https://doi.org/10.1016/j.vaccine.2019.09.001>.
- [36] H. D. Meriki, K. A. Tufon, D. N. Anong, N. J. Tony, T. E. Kwenti, A. F. Bolimo, "Vaccine uptake and immune responses to HBV infection amongst vaccinated and non-vaccinated healthcare workers, household and sexual contacts to chronically infected HBV individuals in the South West Region of Cameroon", *PLoS One*, 13(7), e0200157(2018), DOI: <https://doi.org/10.1371/journal.pone.0200157>.
- [37] M. Lall, S. Sen, S. Patrikar, S. Karade, and R. M. Gupta, "Post vaccination antibody titres of hepatitis B surface antigen (anti-HBs) in a mixed cohort of health care workers", *Med J Armed Forces India*, 78(2), 198-203(2022), DOI: <https://doi.org/10.1016/j.mjafi.2020.11.023>.
- [38] L. Coppeta, A. Pompei, O. Balbi, L. M. Zordo, F. Mormone, S. Policardo, "Persistence of Immunity for Hepatitis B Virus among Healthcare Workers and Italian Medical Students 20 Years after Vaccination" *Int J Environ Res Public Health*, 2019 Apr 29;16(9), 1515(2019), DOI: <https://doi.org/10.3390/ijerph16091515>.
- [39] I. A. Mwangi, J. O. Wesongah, V. M. Musyoki, G. S. Omosa-Manyonyi, B. Farah, L.G. Edalia, "Assessment of hepatitis B vaccination status and hepatitis B surface antibody titres among health care workers in selected public health hospitals in Kenya" *PLOS Glob Public Health*, 3(4), e0001741(2023), DOI: <https://doi.org/10.1371/journal.pgph.0001741>.
- [40] G. H. Lee, and S. G. Lim, "CpG-Adjuvated hepatitis B Vaccine (HEPLISAV-B) Update", *Expert Rev. Vaccines*, 20, 487-95(2021), DOI: <https://doi.org/10.1080/14760584.2021.1908133>.
- [41] S. Schillie, TV. Murphy, M. Sawyer, K. Ly, E. Hughes, R. Jiles, "Durability of antibody response against hepatitis B virus in healthcare workers vaccinated as adults", *Clinical Infectious Diseases*, 60(4), 505–513(2015), DOI: [10.1093/cid/ciu867](https://doi.org/10.1093/cid/ciu867).
- [42] Q. Yuan, F. Wang, H. Zheng, G. Zhang, N. Miao, X. Sun, "Hepatitis B vaccination coverage among health care workers in China", *PLoS ONE*, 14(5), e0216598(2019), DOI: <https://doi.org/10.1371/journal.pone.0216598>.
- [43] P. Zimmermann, and N. Curtis, "Factors That Influence the Immune Response to Vaccination", *Clin Microbiol Rev.*, 32(2), e00084-18(2019), DOI: <https://doi.org/10.1128/cmr.00084-18>.
- [44] S. Yang, G. Tian, Y. Cui, C. Ding, M. Deng, C. Yu, "Factors influencing immunologic response to hepatitis B vaccine in adults", *Sci Rep.*, 6, 27251(2016), DOI: <https://doi.org/10.1038/srep27251>.
- [45] A. Trevisan, A. Giuliani, M. L. Scapellato, S. Anticoli, R. Carsetti, S. Zaffina, "Sex Disparity in Response to Hepatitis B Vaccine Related to the Age of Vaccination", *Int J Environ Res Public Health*, 17(1), 327(2020), DOI: <https://doi.org/10.3390/ijerph17010327>.
- [46] H. V. Sahana, N. Sarala, S. R. Prasad, "Decrease in Anti-HBs Antibodies over Time in Medical Students and Healthcare Workers after Hepatitis B Vaccination" *Biomed Res Int.*, 2017, 1327492(2017), DOI: <https://doi.org/10.1155/2017/1327492>.
- [47] L. S. Chathuranga, F. Noordeen, and A. M. Abeykoon, "Immune response to hepatitis B vaccine in a group of health care workers in Sri Lanka", *International journal of infectious diseases: IJID: official publication of the International Society for Infectious Diseases*, 17, e1078–79(2013), DOI: <https://doi.org/10.1016/j.ijid.2013.04.009>.

- [48] E. Spada, L. Romanò, M. E. Tosti, O. Zuccaro, S. Paladini, M. Chironna, “Study Group. Hepatitis B immunity in teenagers vaccinated as infants: An Italian 17-year follow-up study”, *Clin. Microbiol. Infect.*, 20, 680–6(2014), DOI: <https://doi.org/10.1111/1469-0691.12591> .
- [49] M.G. Bruce, D. Bruden, D. Hurlburt, C. Zanis, G. Thompson, L. Rea, “Antibody Levels and Protection After Hepatitis B Vaccine: Results of a 30-Year Follow-up Study and Response to a Booster Dose”, *J. Infect. Dis.*, 214, 16–22(2016), DOI: <https://doi.org/10.1093/infdis/jiv748> .
- [50] P. Van Damme, M. Dionne, G. Leroux-Roels, O. Van Der Meeren, E. Di Paolo, B. Salaun, P. Surya Kiran, N. Folschweiller, “Persistence of HBsAg-specific antibodies and immune memory two to three decades after hepatitis B vaccination in adults” *J Viral Hepat.*, 26(9),1066-1075(2019), DOI: <https://doi.org/10.1111/jvh.13125> .
- [51] J. Yao, “The response of hepatitis B vaccination on seronegative adults with different vaccination schedules” *Human vaccines immunotherapeutics*, 11 1102–7(2015), DOI: <https://doi.org/10.4161/21645515.2014.985500> .
- [52] M. Nelson, S. R. Mulani, and A. Saguil, “Evaluation of Jaundice in Adults”, *Am Fam Physician*, 111(1), 25-30, PMID: 39823630, (2025).
- [53] I. Ranković, V. Milivojević, A. Pavlović Marković, and M. Bezmarević, “Interplay between chronic hepatitis B and atherosclerosis: Innovative perspectives and theories”, *World J Gastroenterol.* 28(4), 497-499(2022), DOI: <http://dx.doi.org/10.3748/wjg.v28.i4.497> .
- [54] A. Asan, H. Demirhan, H. Ç. Sorkun, S. Ozkan, M. Aydın, D. Akin, “Factors affecting responsiveness to hepatitis B immunization in dialysis patients”, *Int. Urol. Nephrol.*, 49, 1845–50(2017), DOI: <https://doi.org/10.1007/s11255-017-1616-9> .
- [55] G. Vitaliti, A. D. Praticò, C. Cimino, G. Di Dio, E. Lionetti, M. La Rosa, “Hepatitis B vaccine in celiac disease: yesterday, today and tomorrow”, *World J Gastroenterol.*, 19(6), 838-45(2013), DOI: <http://dx.doi.org/10.3748/wjg.v19.i6.838> .