

## ORIGINAL ARTICLE

# Hepatitis B Virus Sero-prevalence and Vaccination Status among Health Care Workers, North East Egypt

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## ABSTRACT

### Key words:

HCWs, Hepatitis B Vaccine, HBV, Egypt

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**Background:** Infection with hepatitis B virus (HBV) is a major worldwide health problem. The estimated prevalence of HBV is about 1.4% in Egypt. This infection is one of the main occupational hazards in the field of health care workers (HCW). **Objectives:** This study aimed to assess the prevalence of HBV infection among HCWs in Suez Canal University Hospital, East Egypt and their hepatitis B vaccination coverage. **Methodology:** A cross sectional descriptive study was conducted, including 450 Health Care Workers (HCWs) with more than 6 months of job experience, selected through stratified random sampling by HCW category. A structured questionnaire was used to collect demographic parameters, history of occupational exposures and HBV vaccination status. Blood samples were screened for HBsAg, hepatitis B core antibody, and hepatitis B surface antibody titer by ELISA. **Results:** Our study sample included 66.7% aged < 30 years. 73.5% of study sample were fully vaccinated, 10.7% were unvaccinated. Only 2.7% of those who have ever been vaccinated had HBsAb testing. There was a significant relation ( $p < 0.001$ ) between occupation and vaccination rate being the highest among nurses and doctors (80%, 78% respectively). Also a significant relationship ( $p < 0.001$ ) was found with education level and age, while no relation was found between gender and vaccination rate. The prevalence of chronic HBV infection and HBcAb were 0.4, and 15.6% respectively. HBV immunity achieved either by healed infection, or evidence of natural boosting was found among 13%. Immunity after vaccination was found in 75%, while 10% were still susceptible to infection. Only 21.1% report injury to infection control office and had viral markers testing. **Conclusion:** Although the use of hepatitis B vaccine decreased the incidence of HBV infection in HCWs, still there is a proportion of healthcare workers are unvaccinated. Therefore, new policies are needed for HBV screening, vaccination, and serological response.

## INTRODUCTION

Hepatitis B infection is a potentially life-threatening liver infection and a major global health problem caused by the hepatitis B virus (HBV). Chronic infection by HBV results in high risk of death from cirrhosis and liver cancer, which resulted in 887,000 deaths in 2015. About 257 million people are estimated infected with HBV (defined by positive serum hepatitis B surface antigen)<sup>1</sup>.

Hepatitis B infection can be transmitted through blood or other body fluids of the infected person. However, infection can be easily prevented by HBV vaccine that is available since 1982, and introduced in Egypt since 1992<sup>2</sup>. The vaccine is safe and highly effective in preventing infection and decreasing the incidence of chronic disease and liver cancer<sup>1</sup>.

According to Egypt Health Issues Survey, 1% (nearly 800,000 persons) and 10% of the Egyptian

general populations were positive for HBsAg and anti-HBc respectively. The percentage of individuals with hepatitis B infection was very low among those under age 20 ( $\leq 0.2\%$ ), that is due to the rapid expansion of hepatitis B vaccination coverage following its addition to the national immunization program in the 1990s, which means that these low hepatitis B infection rates were observed among children and young adults<sup>2</sup>.

The prevalence of HBV infection is highest in the WHO African and Western Pacific Regions, where 6.1% and 6.2% of population, respectively, are infected. In the WHO European, Eastern Mediterranean, and South-East Asia regions, an estimated 1.6%, 3.3% and 2.0% of the general population, respectively, were infected<sup>1</sup>.

The occupational hazards of viral hepatitis for medical and paramedical personnel first received major attention in the American medical literature in 1949

with the report by **Leibowitz et al.**,<sup>3</sup> on a case of blood-bank worker with serum hepatitis.

All workers in the field of health-care who have the potential for exposure to patients and/or to infectious materials, including body substances, contaminated medical equipment, supplies and environmental surfaces are considered health care personnel (HCP). HCP include physicians, therapists, nurses, nursing assistants, pharmacists, dental personnel, technicians, laboratory personnel, and any persons potentially exposed to infectious agents that can be transmitted to and from patients and HCP (e.g., laundry, housekeeping, dietary, administrative, and security)<sup>4</sup>.

In the developing countries, 40%-65% of HBV infections in health-care workers were due to percutaneous exposure. In contrast, this fraction was less than 10%, in developed countries, mainly because of immunization, post-exposure prophylactic measures, and the applied infection control practices<sup>5</sup>.

Prior to the introduction of HBV vaccination, the frequency of HBsAg and anti-HBs among Egyptian health care workers were 3.2% and 28% respectively<sup>6</sup>. More recently, according to study conducted in Tanta(Egypt) among health care workers in governmental and non-governmental hospitals, it was found that 1.4% of Egyptian HCWs were positive for HBsAg and 24.5% were positive for anti-HBc. Worldwide, the frequencies of HBsAg ranges from 0.1-8.1% and anti-HBc ranges from 6.2-73.4% in HCWs<sup>7</sup>.

In the developed world, the risk of occupational transmission of blood borne pathogens is reduced in HCWs is reduced due to firm occupational surveillance that assesses and monitors the health hazards related to blood-borne pathogens and the presence of strict preventive measures. However, in the developing world, exposure and health hazards are rarely assessed or monitored and much remains to be done to protect HCWs from such risks that cause infections, which may in turn impact on the quality of health care<sup>8</sup>.

Evidence about the rate of HBV infection among HCWs in Egypt is scarce, and to better design and target preventive measures, more information is needed about the burden caused by occupational transmissions. Therefore, this study aimed to assess the prevalence of HBV infection among HCWs in Suez Canal University Hospital (east Egypt), and their hepatitis B vaccination coverage, that can minimize the risk of acquiring HBV infection, and estimate the proportion of health care workers susceptible to infection. Evidence from this study may be useful to public health officials in order to plan possible intervention measures.

## METHODOLOGY

This is a cross sectional descriptive study that included 450 health care workers. Subjects were recruited from Suez Canal University teaching Hospital,

Ismailia, Egypt. All health care workers in Suez Canal University Hospital were eligible for participation, and were selected by stratified random sampling. Participants were asked to respond to a questionnaire that includes HBV vaccination history, risk factors for HBV infection and socio-demographic data. According to nature of work, subjects were grouped into 6 categories: Doctors (physicians, surgeons), nurses, paramedical personnel (laboratory technicians, physiotherapists, and radiographers), helpers, medical waste handlers (Service), and others who are not involved directly in patients care (dietary, incinerator and laundry workers). We excluded HCWs with documented immune suppression (HIV-infected persons or persons receiving chemotherapy) or on prolonged steroid therapy.

### **Ethical aspect**

Ethical approval was done by the Suez Canal University, Faculty of Medicine Ethical Committee (approval number 3860). The title, aim, and benefits of the study were explained individually to each subject and, after approval, an informed consent was obtained from each participant.

### **Laboratory testing and HBV screening:**

Five ml of venous blood was collected in sterilized plain tube from all study participants. Serum was separated and stored at  $-20^{\circ}\text{C}$  till starting the analysis day. Samples are tested for HBsAg, anti-HBc, and quantitative detection of anti-HBs using ELISA (Murex HBsAg Version 3, Diasorin, Italy) (Murex anti-HBc - total) (ETI-AB-AUK-3, anti-HBs, Diasorin, Italy). Assays were carried out according to the manufacturer's instructions. Anti-HBs titer of 10 mIU/ml or more was considered protective<sup>9</sup>.

### **Interpretation of hepatitis markers:**

Interpretation of hepatitis markers was done according to the CDC criteria. An individual was considered to have active infection if she is he was positive for HBsAg and HBcAb, resolving infection if HBcAb was only positive, while positive HBsAb was considered a marker of immunity due to vaccination if HBcAb was negative or as a sequence of previous infection if HBcAb was positive<sup>9</sup>.

### **Statistical analysis:**

Statistical analysis was performed using SPSS-17 software (SPSS Inc., Chicago, Illinois, USA). Quantitative data was described in terms of range and mean ( $\pm$ SD), while nonnumeric data were described as frequencies and percentages. Comparison of groups was performed by chi-square test and Student's t test. HBsAb titer was represented as range, median, and geometric mean concentration. Comparison of HBsAb titer between groups was performed by a non-parametric, Kruskal-Wallis test. A value of  $p < 0.05$  was considered statistically significant.

## RESULTS

This study included 450 HCWs from Suez Canal University Hospital, (Table. 1) with 66.7% aged <30 years, including 58.4% nurses, 18.2% doctors, followed by helper and service, 8.7% and 8.2% respectively. Of the 450 HCWs included, 331 (73.5%) were fully vaccinated, 48 (10.7%) were unvaccinated, and 71 (15.8%) didn't complete the full schedule of HBV vaccination (partially vaccinated). Most of the partially vaccinated subjects had missed their 3<sup>rd</sup> dose. The most common causes of incomplete vaccination or not vaccinated at all were: being "Too busy and forgetting" in about 59.7%, followed by "Lack of information about vaccine in 21.8%. Among those who have ever vaccinated, only 2.7% did HBsAb testing.

**Table 1: Distribution of the studied sample according to socio-demographic and professional characteristics (n=450)**

Socio-demographic characteristics	No.	%
<b>Age (years)</b>		
<30	300	66.7
30 – 39	94	20.9
40 – 49	34	7.6
50	22	4.9
Min. – Max.	18.0 – 68.0	
Mean ± SD.	29.70 ± 8.42	
<b>Sex</b>		
Male	166	36.9
Female	284	63.1
<b>Marital status</b>		
Single	182	40.4
Married	248	55.1
Divorced	14	3.1
Widow	6	1.3
<b>Occupation</b>		
Doctor	82	18.2
Nurse	263	58.4
Lab Technician	3	0.7
Radiology Technician	4	0.9
Physiotherapist	7	1.6
Helper	39	8.7
Service	37	8.2
Cooker	7	1.6
Incinerator	2	0.4
Laundry	6	1.3
<b>Education</b>		
Illiterate	28	6.2
Primary	35	7.8
Diploma	99	22.0
Intermediate	159	35.3
Bachelor	110	24.4
Master	16	3.6
Doctoral	3	0.7

Interestingly, from various categories of HCWs, nurses and doctors had the highest vaccination rate (80%, 78% respectively). Vaccination status according to HCWs groups was as follow: nurses (80%), doctors (78%), helpers (64%), Radiology Tech/ Physiotherapist (63.6%), Cooker/ Laundry (61.5%), Incinerator (50%), Service (35%), Lab Technician (33.3%), with a significant relation between occupation and vaccination. (Table 2). Also a significant relationship was found with education level, with increased rate of vaccination among more higher educational level, and the same was observed with age, with higher rate of vaccination among younger age group, as 82.3% of those aged <30 years had complete vaccination, while among those aged ≥50 years, 68.2% were not vaccinated. Likewise, duration of work was significantly related to vaccination rate with higher rate among more less duration of work; ≤5 years 81.9%, and >5-10 years 71.9%. There was no significant relationship between gender and vaccination status (Table 2).

**Table 2: Determinants of vaccination status among HCWs (n=450)**

	Complete vaccination (n=331)		Test of sig.	P
	No.	%		
<b>Age (Years)</b>			$\chi^2=45.266^*$	MC p <0.001*
<30	247	82.3		
30-39	56	59.5		
40-49	21	61.7		
≥50	7	31.8		
<b>Education</b>			$\chi^2=74.916^*$	MC p <0.001*
Illiterate	12	42.8		
Primary	16	45.7		
Diploma	61	61.6		
Intermediate	140	88		
Bachelor	91	82.7		
Master	9	56.2		
Doctoral	2	66.6		
<b>Occupation</b>			$\chi^2=69.248^*$	MC p <0.001*
Doctor	64	78		
Nurse	212	80		
Lab Technician	1	33.3		
Rad Tech/ Physio	7	63.6		
Helper	25	64		
Service	13	35		
Cooker/ Laundry	8	61.5		
Incinerator	1	50		
<b>Duration of work</b>			$\chi^2=37.171^*$	<0.001*
≤5years	209	81.9		
>5-10years	59	71.9		
>10-20years	39	49.4		
≥20 years	24	70.5		
<b>Sex</b>			$\chi^2=1.114$	0.573
Male	120	72.3		
Female	211	74.3		

$\chi^2$ : Chi square test MC: Monte Carlo

\*: Statistically significant at p ≤ 0.05

The prevalence of chronic HBV infection (HBsAg+, anti-HBc+, HBs Ab<10), and anti-HBc positivity were 0.4, and 15.6% respectively. HBV immunity achieved in HCWs either by healed HBV infection, or evidence of natural boosting (HBsAg-, HBcAb+, HBsAb≥10) was found among 13%. Immunity after vaccination (HBsAg-, HBcAb-, HBsAb≥10) was found in 65%, added to them 10% who were fully vaccinated from ≥10

years, so they show decreased HBs Ab level <10, that decreased with time. Those still susceptible to HBV infection comprised 5% of the HCWs (HBsAg-, HBcAb-, HBsAb<10) with no history of full vaccination, also added 5% of persons with history of full vaccination from <10 years, but HBsAb level <10, so they show failure of vaccination. (Table 3, Figure 1).

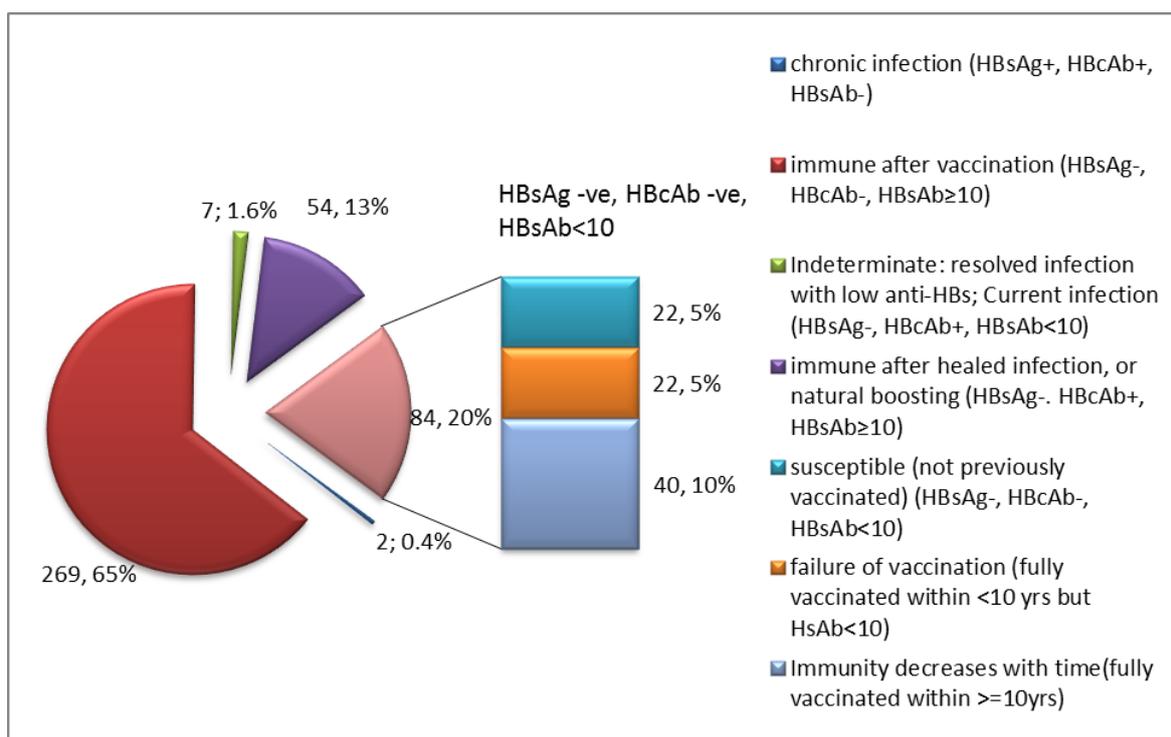


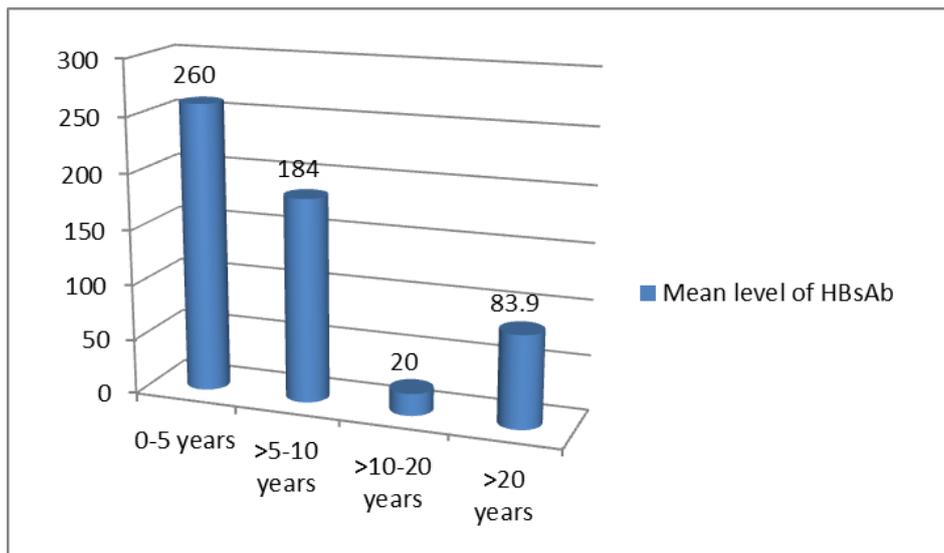
Fig. 1: Interpretation of serologic markers: HBV infection status of HCWs and corresponding percentages (n=450)

Table 3: Interpretation of serologic markers: HBV infection status of HCWs and corresponding percentages (n=450)

Serologic markers			Interpretation	N =450 (%)
HBsAg	HBsAb	HBcAb		
Negative	<10	Negative	Susceptible	44 (10%)
Negative	≥10	Positive	Immune after infection, or natural boosting	54 (13%)
Negative	≥10	Negative	Immune after vaccination	309 (75%)
Positive	<10	Positive	Current infection	2 (0.4%)
Negative	<10	Positive	Indeterminate: <i>possibilities:</i>	7 (1.6%)
			i) Window phase	
			ii) Remote resolved infection with low anti-HBs	
			iii) Chronic infection with low levels of HBsAg	

It was found that 7 participants (1.6 %) had indeterminate results (HBsAg-, HBcAb+, HBsAb<10) with isolated positive anti-HBc resulted from either current infections with low HBsAg titers or long-standing resolved infections with low anti-HBs titers. (Table 3 and Fig. 1). Among the studied sample, 22%

had HBsAb titer <10, 25.6% between 10- 100, and 52.2% with HBsAb titer >100. It was shown that there is a significant decrease in mean level of HBsAb with increasing duration from last dose ( $p = <0.001$ ) (Figure 2).



**Figure 2: Relation of mean level of HBsAb titer with duration from last dose in subjects receiving full vaccination (n =331)**

Protective HBsAb titer ( $\geq 10$ ) was found in 79.8% of subjects who are fully vaccinated, 93.3% of subjects who received 2 doses of vaccine, 73.1% of those who received 1 dose of vaccine, 52.1% who are not vaccinated. (Fig.4) Among the studied sample, 58.2% have ever attended infection control training, and 66.4% have ever exposed to risky situation either brick with infectious sharp, or contact with infected body fluids, with the most common was sharp brick 65.8%.

The most common contributing factor for infection exposure was the careless handling of patient and infectious material 41.8%, or being busy at work 23.3%.

Among those with previous history of exposure, 64.9% wash injured place with antiseptic and water, while only 21.1% reported the event to the infection control office and performed viral markers testing. Risk of HBV infection was assessed in relation different risk factors, (Table 4) shows a significant relationship between previous blood transfusion and acquiring infection, either chronic HBV infection (HBsAg+ve, HBcAb+ve) or current infection (HBsAg-ve, HBcAb+ve, HBsAb<10), with no significant relationship with other factors.

**Table 4: Risk factors for current HBV infection**

	Current HBV infection (HBsAg +ve + HBcAb +ve) (n =2)		HBcAb+ve Unresolved infection { HBsAb<10} (n =7)		Test of sig.	p
	No.	%	No.	%		
<b>Occupation</b>						
Nurse	0	0.0	1	14.3	$\chi^2=4.206$	MC p= 0.724
Physiotherapist	0	0.0	1	14.3		
Helper	1	50.0	0	0.0		
Service	1	50.0	4	57.1		
Incinerator	0	0.0	1	14.3		
<b>Education</b>						
Illiterate	1	50.0	3	42.9	$\chi^2=1.662$	MC p= 1.000
Primary	1	50.0	2	28.6		
Intermediate	0	0.0	1	14.3		
Diploma	0	0.0	1	14.3		
<b>Attending training on infection prevention?</b>						
Yes	1	50.0	3	42.9	$\chi^2=0.032$	FE p= 1.000
No	1	50.0	4	57.1		
<b>Previous needle stick injury?</b>						
Yes	1	50.0	3	42.9	$\chi^2=0.032$	FE p= 1.000
No	1	50.0	4	57.1		
<b>Previous operation?</b>						
Yes	1	50.0	6	85.7	$\chi^2=1.148$	FE p= 0.417
No	1	50.0	1	14.3		
<b>Previous blood transfusion?</b>						
Yes	2	100.0	0	0.0	$\chi^2=9.000^*$	FE p= 0.028*
No	0	0.0	7	100.0		
<b>Previous dentist visiting?</b>						
Yes	2	100.0	5	71.4	$\chi^2=0.735$	FE p= 1.000
No	0	0.0	2	28.6		
<b>Using gloves?</b>						
Yes	2	100.0	3	42.9	$\chi^2=2.057$	FE p= 0.444
No	0	0.0	4	57.1		
<b>Family history of HBV infection?</b>						
Yes	0	0.0	1	14.3	$\chi^2=0.321$	FE p= 1.000
No	2	100.0	6	85.7		

$\chi^2$ : Chi square test      MC: Monte Carlo      FE: Fisher Exact

## DISCUSSION

This study aimed to assess HBV infection prevalence among HCWs in Suez Canal University Hospital, and to estimate Hepatitis B vaccine coverage among them to know the proportion susceptible to HBV infection.

In this study it was found that 0.4% of HCW were positive for HBsAg and 15.6% were positive for anti-HBc. The declining rate of HBsAg among Egyptian HCWs was previously reported in a study conducted between 1986 and 1987 where HBsAg sero-positivity rate was 3.2% among 765 HCWs<sup>6</sup>, whereas in Tanta 1.4% were positive for HBsAg and 24.5% were positive

for anti-HBc<sup>7</sup>, and in Ahmed Maher Hospital, 0.9% were found positive for HBsAg<sup>10</sup>. The findings in the present study indicate that, in the field of healthcare, exposure to HBV infection is significantly high, however, exposure do not progress to chronic infection, mostly due to the adulthood infection. These findings are comparable to that found in Tanzania where 7% had HBsAg positive<sup>11</sup>.

In comparison with a study performed in Alexandria which reported that AntiHBs level decreases significantly in medical students and HCW vaccinated 20 years and  $\geq 5$  years ago respectively. Long term memory was found to be still intact after a booster dose. Long term studies for more than 30 years are important

to assess lifelong immune memory and the need of a booster dose in high risk group <sup>12</sup>.

In this study we found that out of the 450 HCWs included, 73.5% were fully vaccinated, 10.7% were unvaccinated. This percentage of vaccination is higher than studies done in Sudan <sup>13</sup>, Nigeria <sup>14</sup>, Tanzania <sup>11</sup> and India <sup>15</sup> where only 50%, 26.8%, 56.9%, and 56.5% of HCWs were vaccinated respectively. Comparable results were reported in Kuwait where about (74.7%) have received Hepatitis B vaccine <sup>16</sup>. In developed countries, the situation is not much better than our study. According to a study in the United States, 75% of HCWs were vaccinated <sup>17</sup>. In Sweden, only 40% of HCWs were reported to be fully vaccinated <sup>18</sup>. On the other hand, our figure is lower as compared to study done in Italy <sup>19</sup>. This difference of findings between studies might be due to the economic difference of the study populations which causes difficult accessibility and affordability of the vaccine in the developing countries. Also, difference in the level of awareness among HCWs, may be another factor for difference of findings.

In the current study, surveyed HCWs indicated that being "Too busy" followed by "Lack of information about vaccine and HBV" are among the barriers for not being vaccinated, while in a study in Sudan, the unawareness of the vaccine's availability and expensiveness of the vaccine were the main reasons for failure vaccination coverage <sup>13</sup>. This difference in the specified reason of coverage failure might be due to differences in economic difference of the study population and/or difference in the study setting. At the time of the current study, the hospital was applying policies requiring HCWs to be vaccinated against HBV and free HBV vaccination was basically accessible to the hospital staff.

In the present study, in spite of fair vaccination status among HCWs, most of them didn't do immune response test after completing the vaccination schedule. Generally, the efficacy of the vaccine is not 100%, and about 5 to 10 % of the vaccinated subjects will fail to develop immunity against HBV <sup>20</sup>. Accordingly, it is highly important to have immunity test after completing the vaccine schedule in order to identify the non-responders. In our study, only 2.7% of study participants knew about their immune status against HBV, this may be due to the lack of knowledge about the importance of immune response test. This result is inconsistent with the CDC's guidelines for immunization, which require a serologic testing to be done 1–2 months after the last dose of the HBV vaccine <sup>20</sup>.

In the studied sample, 64.2% of the vaccinated HCWs were vaccinated within the last 5 years, whereas 21.9% were vaccinated for more than 20 years. The former showed the effort of the hospital Infection Control Committee (ICC) in the last 5 years regarding

the vaccination of HCWs, while the latter showed the proportion of HCWs vaccinated during childhood according to obligatory vaccination.

The current study stumbled on that completely HBV vaccination was significantly associated with less duration of work ( $\leq 5$  years) and younger age group, mostly due to the higher proportion of younger HCWs included in our study sample who were recently employed, owing to the obligatory vaccination against HBV infection applied in Egypt since 1992. This is comparable to findings from a study in Egypt on 1998 when routine HBV vaccine was not available in the study sites, so that younger HCWs had poorer vaccine uptake or due to their poorer knowledge about their need for HBV vaccination as they are high risk group <sup>21</sup>. Our findings also revealed that complete vaccination coverage was significantly associated with profession group, educational level, and work place. It was found that nurses and doctors were more frequently receiving full vaccination than service, physiotherapists; this is due to the difference in educational level and awareness about HBV and other blood-borne infections and their prevention. Similar results were found in India <sup>15</sup>. But in contrast, in Jeddha, dentists and lab technicians were more predictors for full vaccination than physicians <sup>22</sup>.

Our results are comparable with the findings of studies done in Nigeria <sup>23</sup>, and Saudi <sup>22</sup>, where vaccination coverage among HCWs was linked with longer years of working duration.

In this study, immunity after vaccination (HBsAb titer  $\geq 10$  or HBsAb titer  $< 10$  after 10 years of vaccination) was present in 75 % of workers, while 10 % of them failed to develop immunity against HBV infection. Past healed infection resulted in immunity against HBV in 13 % of the HCWs. Results from Uganda <sup>24</sup>, Tanzania <sup>11</sup>, and India <sup>15</sup>, found a higher proportion of immunity after healed infection and a higher susceptibility ratio, with lower proportion of immunity after vaccination.

The protective level of HBsAb titer decreases with the passage of time after vaccination. Our data show that the HBsAb titers in HCWs who had been vaccinated in the past decline over time. A study conducted in India showed similar results <sup>25</sup>.

Settings that lead to exposure may differ according to the working environment and certain job-related practices. Respondents on our study frequently picked out careless handling of patients or infectious materials as the main contributing factors for exposure to infection, which include injury during recapping or injury from sharp materials while patients suddenly dislodge. After occurrence of the exposure, the most frequently taken measure was washing the injury site with water and antiseptics (64.9%), while in 26% of cases they checked the HBV status of the patient. In this study, most of the exposure events went undocumented. Only 21.1% of respondents have done immediate

reporting. This is inconsistent to CDC's guidelines which states that immediate reporting should be done after sustaining the injury<sup>20</sup>. Similar results were found among surgeons in training in United States<sup>26</sup>, where HCWs didn't report needle stick injury because they didn't want to know the post reporting tests results and others think that reporting was useless.

## CONCLUSION

The risk of hepatitis B infection is well documented among healthcare workers. Although the incidence of HBV infection in HCWs has decreased with the use of hepatitis B vaccine, there is still important scope for improvement, as there is a proportion of healthcare workers are unvaccinated. Therefore, there is a need for well-planned and clear policies for HBV screening, vaccination and serological response checkups for all healthcare workers, especially those who are at a greater risk of exposure to blood or other potentially infectious material and also there is need for booster dose of HBV vaccine for those who are already vaccinated but having anti-HBs titer <10 mIU/ml.

**Conflicts of interest:** The authors declare that they have no financial or non-financial conflicts of interest related to the work done in the manuscript.

- Each author listed in the manuscript had seen and approved the submission of this version of the manuscript and takes full responsibility for it.
- This article had not been published anywhere and is not currently under consideration by another journal or a publisher.

### Author's contribution:

This work was carried out in collaboration between all authors. Nader Nemr conceived and designed the idea, prepared the protocol and revised the final manuscript. Huda Aly and Nashaat Soliman developed the structure, data collection, clinical interpretation and data management. Mohamed Abdalla performed lab work and data management. Fawzy Attia managed literature searches, statistics and data interpretation. Rania Kishk performed lab work, data interpretation, manuscript preparation and submission. All authors reviewed and approved the final manuscript.

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