

Occupational exposure to hepatitis infection among Egyptian healthcare workers and hepatitis B vaccination

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Received 30 January 2016

Accepted 16 May 2016

Journal of The Arab Society for Medical Research 2016, 11:14–21

Background/aim

Healthcare workers (HCWs) are at a high risk for blood-borne pathogens due to their contact with patients and contaminated instruments. The present study aimed to determine the risk of exposure to hepatitis B virus (HBV) and hepatitis C virus (HCV) infections among Egyptian HCWs in relation to the level of infection control education, the number of hepatitis B vaccine doses received, and the resulting immunity.

Participants and methods

This cross-sectional study was conducted on 228 HCWs. Hepatitis B surface antigen, hepatitis B core antibody, hepatitis B surface antibody titer, and hepatitis C virus antibody (HCV-Ab) were tested by using the enzyme-linked immunosorbent assay technique. Real-time PCR for both HBV-DNA and HCV-RNA in serum was done with positive hepatitis B surface antigen and HCV-Ab, respectively.

Results

During the study period, 78% of the HCWs received full HBV vaccination; 73.6% of them were vaccinated in the last 5 years. Lack of protective hepatitis B surface antibody (HBs-Ab) titer was found in 27.2% of the participants. HCV-Ab was positive in 6.14% HCWs, being significantly higher in individuals 40 years of age or older when compared with those under 40. Half of those with positive HCV-Ab had HCV-RNA below the detection limit.

Conclusion

Implementation of infection control guidelines played a role in reducing the prevalence of HCV infection among HCWs and in vaccinating HCWs in the last 5 years. Adopting safety-engineered devices is required to help in the reduction of needle stick and sharp medical devices injuries and risk for blood-borne infections.

Keywords:

healthcare workers, hepatitis B, hepatitis C, infection control measures

J Arab Soc Med Res 11:14–21

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1687-4293

Introduction

The healthcare workers (HCWs) comprise the infrastructure without which the healthcare sector cannot exist. Through caring for patients, HCWs place themselves at a daily risk for contracting life-threatening infections from blood-borne pathogens including hepatitis B virus (HBV) and hepatitis C virus (HCV) [1–4]. Healthcare workforce worldwide represents 12% of the working population with an annual proportion of exposure to blood-borne pathogens: 2.6% for HCV and 5.9% for HBV, corresponding to about 16 000 HCV infections and 66 000 HBV infections worldwide. The risks for transmission of infection from an infected patient to the HCW following needle stick and sharp medical devices injuries (NSSIs) are 3–10% for HBV and 3% for HCV [5].

According to a recent study in the proceedings of the National Academy of Sciences, Egypt has the highest prevalence (14.7%) of HCV. More than 500 000 new HCV infections are reported every year. Therefore,

HCV is considered to be the most significant public health problem in Egypt [6,7]. A study conducted on the occupational exposure to NSSIs and HBV in Egypt (Nile Delta and Upper Egypt) indicated that about 8617 HBV infections occur every year among HCWs in the healthcare environment [8]. The use of safe universal precautions and vaccination of HCWs against HBV are the only means for the prevention of hepatitis B among HCWs [9]. A study carried out among Egyptian HCWs in a national liver disease referral center detected a prevalence of hepatitis C virus antibody (HCV-Ab), hepatitis B surface antigen (HBs-Ag), and coinfection as 16.6, 1.5, and 0.2%, respectively [10].

Existing information about the effect of increasing awareness to infection control guidelines

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implemented in hospitals, hepatitis B vaccination in relation to existing immunity, and other risk factors for exposure to blood-borne infections with their effect on the seroprevalence rate of HBV and HCV infection among HCWs still needs to be evaluated.

The purpose of this study was to determine the seroprevalence of HBV and HCV infections among a sample of Egyptian HCWs at Ahmad Maher Teaching Hospital in relation to their different occupations and other risk factors. The rate of vaccinated HCWs to HBV and their resulting immunity were also evaluated.

Participants and methods

This cross-sectional study was conducted from January 2013 to October 2013 on a group of the HCWs at Ahmed Maher Teaching Hospital, one of the hospitals of the General Organization of Teaching Hospitals and Institutes in Cairo, Egypt, after obtaining the approval of the ethical committee from the General Organization of Teaching Hospitals and Institutes. Written consent from all the included HCWs was obtained.

The data were collected via interview-based precoded questionnaire, which was carefully designed to meet the objectives of the study; it included age, sex, job category, duration of working in medical field, and hepatitis B vaccination (duration in addition to the number of doses received). Risk factors for HBV and HCV transmission at hospital (the most common of which are NSSIs and accidental exposure to blood and body fluids), beside other related risk factors as history of previous operations, blood transfusion, blood donation, dentists visiting, and awareness to gloves use were also included. The total number of study participants was 228, including 24 workers, 69 nurses, 43 lab personals (technicians and doctors), 48 internal medicine doctors, and 44 surgeons. All the included individuals were from urban areas and none of them had a history of bilharziasis. All enzyme-linked immunosorbent assay (ELISA) laboratory tests were performed on serum.

Sera collection, preparation, and storage

A volume of 1.5 ml serum and 1.5 ml plasma were separated aseptically from blood of each HCW by centrifugation and were divided into two aliquots of serum and two aliquots of plasma to prevent repeated freezing and thawing of the same aliquot. Only clearly nonhemolyzed specimens were used. Sera were coded and stored at -70°C till processing. Sera were brought

to room temperature before testing. Frozen specimens were completely thawed and mixed well before testing.

Detection of HBs-Ag

Detection of HBs-Ag was carried out using (Axiom GmbH, Bürstadt, Germany) the ELISA technique. Positive results were repeated. No equivocal results were noted.

Detection of anti-HBc

It was done using (Biokit S.A., Barcelona, Spain) the ELISA technique, which is a competitive test. The presence of hepatitis B core antibodies (anti-HBc) was determined by using the recorded absorbance and comparison with the calculated cutoff values. Samples with an optical density less than the cutoff values were considered as positive. Samples with optical density higher than the cutoff values were considered as negative. Positive samples were retested in duplicate before final interpretation. Four equivocal results were noted and when repeated in duplicate showed negative results.

Detection and quantification of HBs-Ab titer

It was done using (Biokit S.A.) the ELISA quantitative technique. Plotted in linear-linear graphic coordinates, the anti-HBs concentrations of the negative control (0 mIU/ml), low positive calibrator (10 mIU/ml), and high positive calibrator (100 mIU/ml) were plotted on the abscissa (x -axis) against their corresponding mean absorbance values on the ordinate (y -axis). A line was drawn through these three points. The concentration in mIU/ml of each sample was derived from its absorbance using the calibration curve.

Detection of HCV-Ab

It was done using (Axiom GmbH) the third generation ELISA technique.

Real-time PCR

DNA was extracted from 200 μl of plasma from HBs-Ag positive HCWs with a DNA extraction kit, catalog no. 57704, and RNA was extracted from 140 μl of plasma from HCWs HCV-Ab positive with a viral RNA mini kit, catalog no. 52904, according to the manufacturer's guidelines (QIAGEN GmbH, Germany).

Quantitative detection of HCV-RNA and HBV-DNA by using real-time PCR

Using real-time PCR, the amplified product was detected by using fluorescent dyes. These were usually linked to oligonucleotide probes that bind specifically to the amplified product. Monitoring the

fluorescence intensities during the PCR run (i.e. in real-time) allowed the detection and quantitation of the accumulating product without having to re-open the reaction tubes after the PCR run [11].

Detection of HBV-DNA was performed on a Step One Real-Time PCR system (Applied Biosystems, California, USA) using a ready-to-use PCR kit supplied by artus HBV PCR kit 24, version 1, catalog no. 4506163 (QIAGEN GmbH). The HBV RG/TM Master contained reagents and enzymes for the specific amplification of a 134bp region of the HBV genome. The amplicons were detected by measuring the FAM fluorescence in the ABI PRISM SDS, Applied Biosystems', California, USA.

The kit contained a second heterologous amplification system to identify possible PCR inhibition. This was detected as an internal control by measuring the JOE fluorescence. In addition, external positive controls (HBV RG/TM QS 1–5) were supplied, which allowed the determination of the pathogen load. The quantitation standards were treated as previously purified samples and the same volume (20 µl) were used to generate a standard curve on an ABI SDS. Detection limit was 16 IU/ml.

Detection of HCV-RNA was carried out on a Step One Real-Time PCR system (Applied Biosystems)

using a ready-to-use PCR kit supplied by artus HCV RG RT-PCR Kit 24, version 1, catalog no. 4518263 (QIAGEN GmbH). The HCV RG Master A and B contain reagents and enzymes for the reverse transcription and specific amplification of a 240bp region of the HCV genome, and for the direct detection of the specific amplicon in fluorescence channel Cycling Green.

In addition, the artus HCV RG RT-PCR kit contains a second heterologous amplification system to identify possible PCR inhibition. This is detected as an internal control in fluorescence channel Cycling Orange, in addition to the external determination of the pathogen load. The quantitation standards were treated as previously purified samples and the same volume (20 µl) was used to generate a standard curve on an ABI SDS. Detection limit is 36 IU/ml.

Statistical methods

Statistical analyses were carried out by using the SPSS, version 18 (SPSS Inc., Chicago, Illinois, USA). Qualitative results were expressed as number and percentage. The qualitative results were analyzed using Pearson's χ^2 -test; furthermore, likelihood ratio was used for cases with more than 25% of the cells with an expected count less than 5. The association was studied through odds ratio, with a confidence interval of 95%. A *P*-value of less than 0.05 was considered

Table 1 HBs-Ab titer, HBs-Ag, anti-HBc, and HCV-Ab according to the age of the of HCWs

	Age [n (%)]		P-value
	HCWs < 40 years (n = 146)	HCWs ≥ 40 years (n = 82)	
HBs-Ab titer (mIU/ml)			
<10	37 (25.30)	25 (30.50)	0.03
10<50	23 (15.80)	18 (22.00)	
50	14 (9.60)	7 (8.50)	
100	17 (11.60)	17 (20.70)	
>100	55 (37.70)	15 (18.30)	
HBs-Ab titer (cut point 10 mIU/ml)			
<10	37 (25.3)	25 (30.5)	0.402
≥10	109 (74.7)	57 (69.5)	
HBs-Ag			
Negative (n = 226)	145 (99.30)	81 (98.80)	0.684*
Positive (n = 2)	1 (0.70)	1 (1.20)	
Anti-HBc			
Negative (n = 200)	131 (89.70)	69 (84.10)	0.218
Positive (n = 28)	15 (10.30)	13 (15.90)	
HCV-Ab			
Negative (n = 214)	143 (97.90)	71 (86.60)	0.001
Positive (n = 14)	3 (2.10)	11 (13.40)	

Anti-HBc, hepatitis B core antibody; HBs-Ab, hepatitis B surface antibody; HBs-Ag, hepatitis B surface antigen; HCV-Ab, hepatitis C virus antibody; HCWs, healthcare workers.

*Likelihood ratio is used in the analysis.

statistically significant. All the results were tabulated and the suitable figures were illustrated.

Results

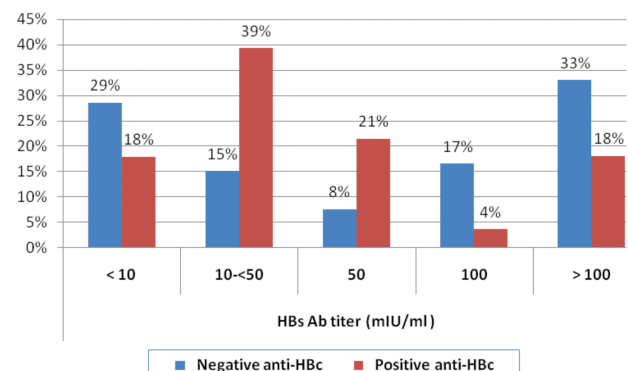
The results tabulated in Table 1 show that there were significant differences in the percentages of HCWs aged less than 40 years and the HCWs more than or equal to 40 years of age, according to their HBs-Ab titer. There was a significant difference in the distribution of HCWs according to the HBs-Ab titer between the two age groups. The percent of HCWs aged under 40 years with positive HBs-Ab titer more than 100 mIU/ml were much higher than the percent of those aged more than or equal to 40 years. Whereas, there was no significant difference between the two age groups as regards other HBs-Ab titers. As regards HBV infection, there was no significant difference between the percent of the HCWs aged under 40 years and those aged more than or equal to 40 years in relation to positive HBs-Ag and anti-HBc. As regards HCV infection, HCV-Ab percent in HCWs with age more than or equal to 40 years was significantly higher compared with those with age under 40 years.

The results tabulated in Table 2 show that there were no significant differences between the percentages of HCWs with the different occupational tasks according to the results of HBs-Ab titer, anti-HBc, HBs-Ag, and HCV-Ab.

In Figure 1, out of the HCWs with positive anti HBc 18% did not develop protective titer of HBs-Ab titer (their titers were less than 10 mIU/ml, while 29% of the HCWs with negative anti-HBc developed HBs-Ab titer more than 100 mIU/ml. HCWs with negative anti-HBc, who developed HBs-Ab titer more than 100 mIU/ml, were 33% compared with 18% HCWs with positive anti-HBc.

Figure 2 illustrates the HBs-Ab titer in the vaccinated personnel according to the number of doses of vaccine received, showing significant difference between the two groups ($P < 0.0001$). There was a significant increase in the percent of HCWs with HBs-Ab titer more than 100 mIU/ml among those fully vaccinated

Figure 1



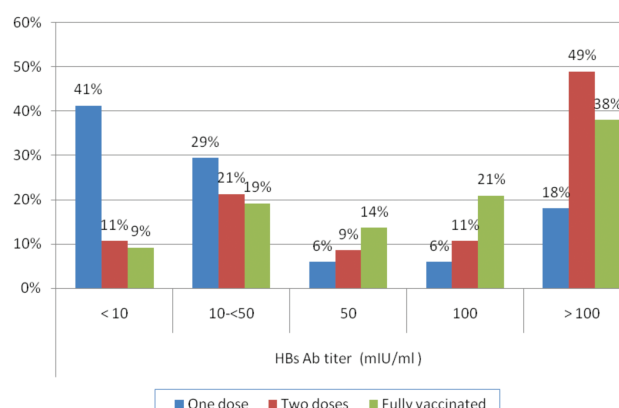
Comparison of the percent of the HCWs with positive and negative anti-HBc according to HBs-Ab titer. Anti-HBc, hepatitis B core antibody; HBs-Ag, hepatitis B surface antigen; HCWs, healthcare workers.

Table 2 HBs-Ab titer, HBs-Ag, anti-HBc, and HCV-Ab according to the occupations of the studied sample of HCWs

	Workers (<i>n</i> =24) [<i>n</i> (%)]	Nurses (<i>n</i> =69) [<i>n</i> (%)]	Laboratory personnel (<i>n</i> =43) [<i>n</i> (%)]	Internal medicine (<i>n</i> =48) [<i>n</i> (%)]	[<i>n</i> (%)]	<i>P</i> -value
HBs-Ab titer						
0 to <10	7 (29.2)	16 (23.2)	13 (30.2)	9 (18.8)	17 (38.6)	0.619
10 to <50	3 (12.5)	13 (18.8)	6 (14.0)	12 (25.0)	7 (15.9)	
50	3 (12.5)	6 (8.7)	2 (4.7)	7 (14.6)	3 (6.8)	
100	4 (16.7)	11 (15.9)	4 (9.3)	8 (16.7)	7 (15.9)	
>100	7 (29.7)	23 (33.3)	18 (41.9)	12 (25)	10 (22.7)	
HBs-Ag						
Negative (<i>n</i> =226)	24 (100.0)	69 (100.0)	42 (97.7)	47 (97.9)	44 (100.0)	0.549
Positive (<i>n</i> =2)	0 (0.0)	0 (0.0)	1 (2.3)	1 (2.1)	0 (0.0)	
Anti-HBc						
Negative (<i>n</i> =200)	19 (79.2)	61 (88.4)	40 (93.0)	41 (85.4)	39 (88.6)	0.549
Positive (<i>n</i> =28)	5 (20.8)	8 (11.6)	3 (7.0)	7 (14.6)	5 (11.4)	
HCV-Ab						
Negative (<i>n</i> =214)	22 (91.7)	67 (97.1)	38 (88.4)	47 (97.9)	40 (90.9)	0.219
Positive (<i>n</i> =14)	2 (8.3)	2 (2.9)	5 (11.6)	1 (2.1)	4 (9.1)	

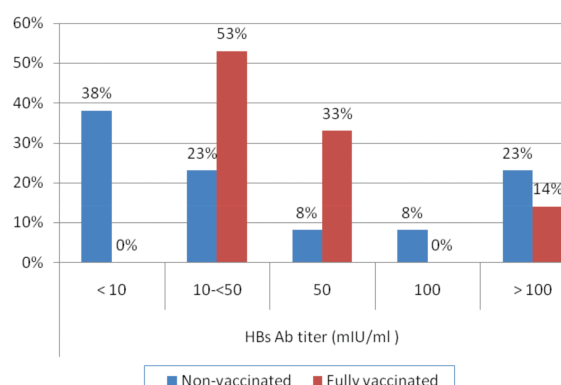
Anti-HBc, hepatitis B core antibody; HBs-Ag, hepatitis B surface antigen; HBs-Ab, hepatitis B surface antibody; HCV-Ab, hepatitis C virus antibody; HCWs, healthcare workers.

Figure 2



Comparisons of the HBs-Ab titer according to the doses of vaccination in the vaccinated HCWs. HBs-Ab, hepatitis B surface antibody; HCWs, healthcare workers.

Figure 4



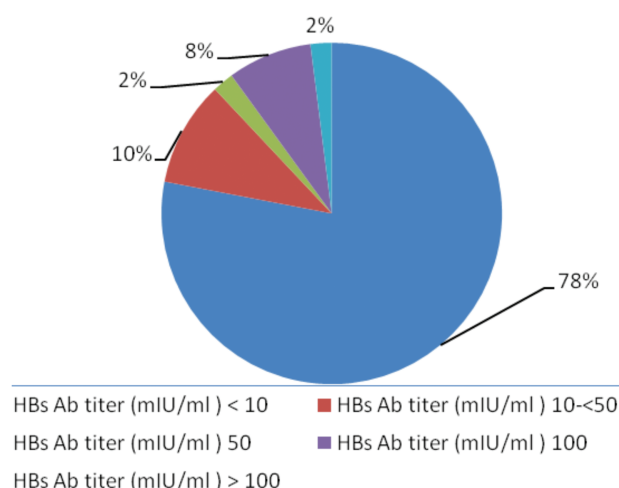
Comparison of the HBs-Ab titer between the fully vaccinated and the nonvaccinated HCWs among those with positive anti-HBc. Anti-HBc, hepatitis B core antibody; HBs-Ab, hepatitis B surface antibody; HCWs, healthcare workers.

compared with the other HCWs. Fig. 3 shows that 78% of the nonvaccinated persons were with HBs-Ab titer less than 10 mIU/ml.

Figure 4 illustrates the comparison between the percentages of fully vaccinated and not-fully vaccinated HCWs with positive anti-HBc according to their HBs-Ab titer, as there was a significant difference ($P < 0.0001$). There was a marked increase in the percent of HCWs with HBs-Ab titer less than 10 mIU/ml among nonvaccinated HCWs, whereas the HBs-Ab titer of the fully vaccinated HCWs was above 10 mIU/ml.

Table 3 shows that the significant risk factors for HBs-Ag were blood transfusion, operations, and blood donation, which were similar for anti-HBc in addition to repeated NSSIs. Blood transfusion,

Figure 3



Distribution of HCWs not vaccinated according to their HBs-Ab titer. HBs-Ab, hepatitis B surface antibody; HCWs, healthcare workers.

blood donation, and gloves awareness were the significant risk factors for HCV-Ab.

Table 4 shows that the age of the HCWs had no significant effect on gloves awareness. Moreover, occupational tasks had significant impact on the negative behavior of the HCWs toward gloves awareness. The negative behavior toward gloves use was higher among the workers.

Figure 5 illustrates the distribution of the quantitative PCR among the examined PCR-positive HCWs, showing that 50% of the examined PCR were below the detection limit of the kit and that most of the positive PCR were between 36 and 100 000 IU/ml.

Discussion

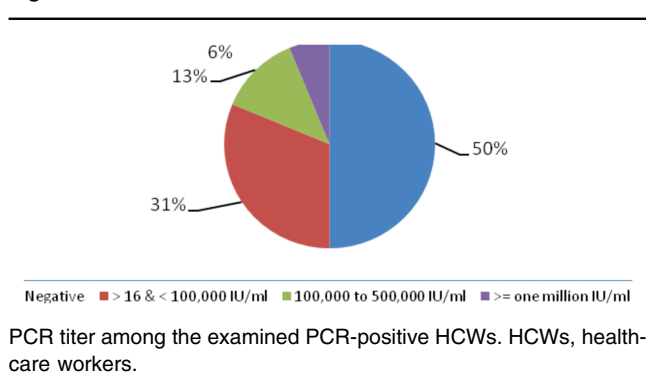
HBs-Ab is the only easily measurable parameter that correlates with vaccine-induced protection. Immunocompetent persons who achieve HBs-Ab concentrations up to 10 mIU/ml after having received a complete more than or equal to three dose of hepatitis B vaccine are considered seroprotected and deemed vaccine responders [12]. Antibodies to HBc, whether of class immunoglobulin M or immunoglobulin G, do not neutralize the virus but only identify all previously infected persons [13]. HCWs in the current study who had positive anti-HBc (12.3%, 28 out of 228) were divided to two subgroups: a subgroup of fully vaccinated ($n=16$) HCWs and the other subgroup including those who did not receive any dose of vaccine ($n=8$). Resolved hepatitis B infection

Table 3 The risk factors for HBs-Ag, anti-HBc, and HCV-Ab in the examined HCWs

	HBs-Ag		Anti-HBc		HCV-Ab	
	OR	CI	OR	CI	OR	CI
Blood transfusion	1.4	0.88–2.24	3.0	0.56–16.26	2.67	0.29–23.83
Operation	1.02	0.99–1.05	1.79	0.80–3.98	0.93	0.31–2.78
NSSIs >2 times	0.08	0.96–1.01	1.02	0.46–2.25	4.03	0.88–18.46
Blood donor	1.03	0.99–1.08	1.19	0.51–2.78	0.18	0.02–1.38
Dentist visits	0.98	0.95–1.01	0.47	0.21–1.05	0.67	0.22–2.04
Gloves awareness	0.17	0.01–2.80	0.78	0.28–2.22	5.71	2.14–15.24

Table 4 Awareness of healthcare workers according to their age and their different occupations

	Negative [n (%)]	Weak [n (%)]	Positive [n (%)]	P-value
Gloves awareness				
Age (years)				
<40 (n=146)	5 (3.40)	14 (9.60)	127 (87.00)	0.675
≥40 (n=82)	3 (3.60)	12 (14.60)	67 (81.70)	
Occupation				
Workers (n=24)	3 (12.50)	4 (16.70)	17 (70.80)	0.03
Nurses (n=69)	3 (4.30)	7 (10.10)	59 (85.50)	
Laboratory personnel (n=43)	2 (4.60)	9 (20.90)	32 (74.40)	
Medical doctors (n=48)	0 (0.00)	5 (10.40)	43 (89.60)	
Surgeons (n=44)	0 (0.00)	1 (2.30)	43 (97.70)	

Figure 5

detected by positive anti-HBc and negative HBs-Ag did not offer an efficient protective HBs-Ab titer among our study sample, which might be due to waning effect of the titer (Fig. 4). Vaccination being safe even in several doses [14,15], HCWs could be vaccinated regardless being previously infected or not, guided mainly by HBs-Ab titer.

The studied sample of HCWs at Ahmad Maher Teaching Hospital showed that 22% (50 out of 228) had never received any dose of the vaccine and 78% of them had no HBs-Ab titer (Fig. 3), thus were vulnerable to hepatitis B infection. A total of 27.2% of the whole studied sample (62 out of 228) was lacking protective HBs-Ab titer, whether they were nonvaccinated ($n=39$) or had not received the full

vaccination dose ($n=23$). HCWs with less than 10 mIU/ml HBs-Ab titer did not only include nonvaccinated HCWs but also included 41% of HCWs who received only one dose, 11% of those who received two doses, and 9% of those who were fully vaccinated (Fig. 2), thus showing a variable response to vaccination. Postvaccination seroprotection was achieved in 92% of the HCWs aged under 40 years and 84% of HCWs aged more than or equal to 40 years. All members of the group with less than 10 mIU/ml HBs-Ab titer were sent back to the hospital Infection Control Committee (ICC) with a laboratory recommendation to receive one or three doses of the vaccine (according to their history) and were asked to come back to the laboratory after 1–2 months so as to re-assess their antibody titer [14].

Overall, 18% of the HCWs who had documented vaccination less than 5 years ago at the hospital ICC had HBs-Ab titer less than 10 mIU/ml (Fig. 1). This shows the importance of measuring the HBs-Ab titer following full vaccination because of various responses to hepatitis B vaccine among different individuals, ranging from nonresponders to weak or effective response. Checking of titer should be compulsory for HCWs [16], as recently the Centers for Disease Control and Prevention declared that once the protective titer is attained by the HCW, the vaccine is immune and further serologic testing or vaccination is not needed

[17]. In the studied sample, 73.6% of the vaccinated HCWs were vaccinated within the last 5 years, whereas 26.4% were vaccinated for more than 5 years or even more. The latter showed the effort of the hospital (ICC) in the last 5 years regarding the vaccination of HCWs.

Negative behavior toward the use of gloves was significantly high among the workers compared with individuals of other occupations (Table 4), which might be attributed to the level of education among the workers, who thus require more educating, training, and follow-up.

Occupational exposure to percutaneous injuries and NSSIs are a substantial source of infections with blood-borne pathogens among HCWs causing substantial health consequences and psychological stress for them [18,19], and accounts for almost 40% of the HCV infections [20]. In the current study, laboratory personnel formed the highest proportion among those who did not have any previous NSSIs (49%). On the other hand, the surgeons and the workers were repeatedly exposed to NSSIs (more than three times, 64 and 58%, respectively). The nurses were either never been exposed to NSSIs (44%) – some of whom might be denying – or had been repeatedly exposed to NSSIs (46%). Other risk factors for HBV and HCV infections were considered in this study; such as previous history of exposure to operations, blood transfusion, blood donation, and visiting dentist. Table 3 shows that the significant risk factors for both chronic HBV and resolved B infection were blood transfusion, blood donation, undergoing operations, and repeated NSSIs. For HCV infection, blood transfusion, blood donation, and gloves awareness were the significant risk factors. This was in agreement with another study at the Egyptian National Liver Diseases Referral Center that showed that HCV infection among HCWs was more likely to be community acquired and not occupationally related [10].

As regards HBV infection, no significant difference was detected in relation to age, whether in those with resolved infection or those with chronic infection. Nevertheless, Egypt has been recorded with an intermediate range of HBV prevalence as 2–8% [15]. Our study sample showed only two HCWs with chronic infection (0.9%). HCV infection among the studied sample was 6.14% (14/228), as shown in Table 1, showing lower prevalence than that reported by Centers for Disease Control and Prevention in Egypt (>10%) [21]; similarly, a study conducted at the Egyptian National Liver Diseases

Referral Center showed 16.6% prevalence among HCWs [10]. HCV-Ab prevalence in HCWs aged more than or equal to 40 years was significantly higher compared with those with less than 40 years. There was no significant difference in relation to the different occupations; highest prevalence was found among laboratory personnel and surgeons (Table 2). A Mexican study declared that among HCWs, nurses were most commonly exposed to infection (41%), followed by physicians (31%) [22].

Quantitative HCV-RNA for HCV-Ab positive HCWs showed different values of HCV-RNA number in serum, with half of them (seven out of 14) having undetectable level of HCV-RNA. Only one of the HCWs (1/14, 7.14%) had a high level of HCV-RNA (more than one million HCV-RNA, IU/ml in serum), and the other six had HCV-RNA lower than 500 000 IU/ml (Fig. 4). Similarly, quantitation of HBV-DNA for the two HCWs with chronic B infection showed one of the two with undetectable level of HBV-DNA. No coinfection was detected in the studied individuals.

All positive cases of HCWs were referred with their ELISA and quantitative real-time PCR in serum results to the hospital Hepatology Department to be followed and treated by a specialist or to refer to their medical insurance. Confidentiality of every HCWs' results was maintained.

Conclusion

The study concluded that the implementation of infection control guidelines played a role in reducing the prevalence of HCV infection among HCWs and in vaccinating HCWs in the last 5 years. Adopting safety-engineered devices is required to help in the reduction of NSSIs and risk for blood-borne infections.

Conflicts of interest

There is no conflict of interest.

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