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MINIREVIEWS

## Hepatitis B virus and hepatitis C virus infection in healthcare workers

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#### Abstract

Approximately 3 million healthcare workers per year receive an injury with an occupational instrument, with around 2000000 exposures to hepatitis B virus (HBV) and 1000000 to hepatitis C virus (HCV). Although an effective HBV vaccine has been available since the early eighties, and despite the worldwide application of universal vaccination programs started in the early nineties, HBV still remains a prominent agent of morbidity and mortality. There is no vaccine to limit the diffusion of HCV infection, which progresses to chronicity in the majority of cases and is a major cause of morbidity and mortality worldwide due to a chronic liver disease. Healthcare workers are frequently exposed by a mucosal-cutaneous or percutaneous route to accidental contact with human blood and other potentially infectious biological materials while carrying out their occupational duties. Mucosal-cutaneous exposure occurs when the biological material of a potentially infected patient accidentally comes in contact with the mucous membranes of the eyes or mouth or with the skin of a healthcare worker. Percutaneous exposure occurs when an operator accidentally injures himself with a sharp contaminated object, like a needle, blade or other sharp medical instrument. About 75% of the total occupational exposure is percutaneous and 25% mucosal-cutaneous, the risk of infecting a healthcare worker being higher in percutaneous than in mucosal-cutaneous exposure. All healthcare workers should be considered for HBV vaccination and should meticulously apply the universal prophylactic measures to prevent exposure to HBV and HCV.

**Key words:** Hepatitis B virus infection; Hepatitis C virus infection; Needle-stick injury; Healthcare workers

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Core tip: Preventing the transmission of hepatitis B virus



(HBV) or hepatitis C virus infection from source patients to healthcare workers is of vital importance in all healthcare settings worldwide, since these workers are exposed daily to these infections over a period of almost four decades. Needle pricks with contaminated needles, cuts from sharp instruments and blood splashes to the conjunctiva are the most frequent causes of exposure, injuries largely preventable by taking the standard universal precautions. HBV vaccination of anti-HBs-negative healthcare workers is recommended in all countries, but numerous healthcare workers remain exposed to infection because they have eluded HBV vaccination.

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#### INTRODUCTION

Hepatitis B virus (HBV) and hepatitis C virus (HCV) are responsible for the two most widespread forms of chronic hepatitis worldwide<sup>[1-3]</sup>. Healthcare workers are exposed to the risk of acquiring HBV and HCV infection through mucosal-cutaneous exposure (eyes or mouth mucosa or skin) to potentially infectious blood or blood products or through percutaneous exposure to contaminated sharp objects (needles, blades, etc.). Twenty-five percent of the total occupational exposure is mucosal-cutaneous and 75% percutaneous<sup>[4]</sup>. The risk of HBV or HCV infecting a healthcare worker is higher in percutaneous than in mucosal-cutaneous exposure. According to the data provided by the World Health Organization (WHO), there are approximately 36 million healthcare workers worldwide, of whom around 3 million per year receive an injury with a sharp instrument, thus resulting in 2000000 subjects contaminated with HBV and 1000000 with HCV<sup>[4]</sup>. Other studies estimated that the incidence of injuries to healthcare workers caused by sharp objects ranges from 1.4 to 9.5 per 100 healthcare workers per year, resulting in 0.42 HBV infections per 100 sharp-object injuries per year<sup>[5]</sup>.

This review article will focus on the risks of healthcare workers acquiring HBV and HCV chronic infections while carrying out their occupational duties.

#### **HBV INFECTION**

HBV infection is a global health problem since 240 to 350 million<sup>[6-9]</sup> people worldwide are estimated to be chronically infected, of whom 312000 die annually of advanced cirrhosis and 341000 of liver cancer<sup>[7]</sup>.

Ten genotypes of HBV have been identified to date, from A to J, based on a genetic diversity of at least 8% in the viral genome<sup>[10,11]</sup>. HBV genotypes show a peculiar

geographical distribution<sup>[12]</sup>. Genotype A predominates in Northern Europe and North America, genotypes B and C in central Asia, genotype D in Mediterranean countries, genotype E in sub-Saharan Africa and in Madagascar, genotype F in South and Central America, genotypes G and H in Mexico and some countries in Central America<sup>[13,14]</sup> and genotypes I and J in Eastern Asia<sup>[15]</sup>.

The age at the time of infection modulates the progression to chronicity of HBV infection, which occurs in around 90% of babies born to hepatitis B e antigen (HBeAg)-positive mothers, a rate that progressively decreases with the increase in age up to 2%-5% in the adult population<sup>[16]</sup>.

The endemicity of HBV infection in a geographical area is classified according to the prevalence of subjects with hepatitis B surface antigen (HBsAg) positivity in the general population as, high (> 8%), intermediate (2.0%-7.9%) and low  $(< 2\%)^{[11]}$ . These categories reflect the predominant patterns of transmission and outcomes of HBV infection. In geographical areas with a high HBV endemicity, such as some countries in Eastern Asia or in sub-Saharan Africa, the majority of HBsAgpositive individuals acquired HBV infection at birth or in early childhood, when the risk of progression to chronicity is very high<sup>[7,15]</sup>. In geographical areas with an intermediate HBV endemicity, such as countries in Northern Africa, the Middle East and Southern Asia, and Eastern Europe, the majority of HBsAg-positive subjects acquired HBV infection in childhood or early adulthood, and family transmission plays an important role in the spread of HBV infection. Finally, in most countries in Western Europe, North, Central and South America and Australia the prevalence of HBsAg-positive individuals is below 2%<sup>[6,7,14]</sup>, the impact of vertical and horizontal transmission in childhood is low, and most HBsAgpositive individuals acquired HBV infection through sexual contact, intravenous drug use (IVDU) or other parenteral exposure to infected blood<sup>[17,18]</sup>.

#### **HCV INFECTION**

HCV infection progresses to chronicity in 70% of cases, a condition that may lead to liver cirrhosis and hepatocellular carcinoma<sup>[19,20]</sup>. According to a WHO report<sup>[21]</sup>, 130-150 million people are chronically infected with HCV. HCV epidemiology shows considerable regional differences. In some geographical areas the endemicity is high, with more than 3.5% of the population having an HCV chronic infection, such as some countries in the Middle East and Central and Eastern Asia and Northern Africa. Several countries in Southern Asia, sub-Saharan Africa, the Andean territories, Central and South America, the Caribbean area, Oceania, Australasia and central and Eastern Europe have a moderate endemicity, with 1.5%-3.5% of subjects carrying HCV infection. The areas considered at low endemicity (< 1.5% of HCV chronic carriers) include countries in the Asian Pacific regions, tropical Latin America, North America and Western Europe<sup>[22]</sup>.



HCV strains have been classified to date into seven genotypes, namely from 1 to 7, on the basis of phylogenetic and sequence analyses of the whole viral genome<sup>[23]</sup>. The global geographical distribution of HCV genotypes is complex. HCV genotype 1 is the most prevalent worldwide, comprising 83.4 million cases (46.2% of all HCV chronic carriers), of whom approximately one-third live in Eastern Asia. HCV genotype 3 is the second most prevalent, and genotypes 2, 4 and 6 are responsible for the majority of the remaining cases worldwide. Eastern Asia has the largest number of carriers with genotype 2 and genotype 6, while Northern Africa and the Middle East have the largest number of carriers with genotype 4. HCV genotype 5 is responsible for around 1.4 million chronic infections (< 1% of all HCV cases worldwide), of which the vast majority in Southern and Eastern sub-Saharan Africa<sup>[22-26]</sup>. Worthy of note, HCV genotypes 1 and 3 generally predominate irrespective of the economic status, while the largest proportions of chronic carriers of HCV genotypes 4 and 5 live in low-income countries.

## RISK FACTORS FOR THE ACQUISITION OF HBV AND HCV INFECTION

HBV circulates in peripheral blood of infected subjects and any parenteral or mucosal exposure to potentially infected blood or blood contaminated material can be considered a risk for HBV transmission to non-immune/ non-infected subjects<sup>[18,27]</sup>. In addition, the virus is present at infectious concentrations in semen and cervical secretions, and, consequently, HBV is frequently transmitted also by sexual and vertical routes<sup>[8,16]</sup>. The impact of the various routes of transmission varies significantly from one country to another<sup>[8,16]</sup>. In countries with a high endemicity level, HBV infection is prevalently acquired at birth from an HBeAq-positive mother, in which case it becomes chronic in around 90% of cases, or by horizontal transmission in early childhood through household contact, with a progression to chronicity from 10% to 40% of cases. Promiscuous unprotected sexual activity and IVDU are the major risk factors for acquiring HBV infection in areas with a lowprevalence, such as the United States<sup>[28]</sup>.

Worthy of note, the screening of blood donors for markers of HBV infection has dramatically reduced the risk of HBV transmission through the transfusions of blood and blood products. At present, this risk is estimated as 1-4 cases per million blood components transfused in low-prevalence areas<sup>[29]</sup> and around 1 case per 20000 blood transfusions in high-prevalence regions<sup>[30]</sup>.

The transfusion of infected blood and blood products was the most prominent route of transmission of HCV infection until 1989<sup>[1,31]</sup>. Routine mandatory screening of blood donors for circulating antibodies to HCV that started in the early 1990s has drastically reduced the risk of HCV transmission due to the transfusion of blood and

blood products, currently estimated between 1/500000 and 1/1000000 blood units[32]. Some concern for HCV transmission through blood transfusion remains only for some geographical areas with limited resources<sup>[33]</sup>. In developed countries, the sharing of injection equipment among IVDUs is one of the major risk factors for the acquisition of HCV infection, as demonstrated by the high anti-HCV seroprevalence found (70% or more in some studies) in this subset of subjects[34]. Conversely, in low-income countries, HCV transmission is frequently due to re-using equipment for injection and other inadequately sterilized therapeutic instruments<sup>[35]</sup>. HCV is rarely acquired through sexual intercourse<sup>[36]</sup>, but some outbreaks of acute HCV infections occurring in men having sex with men in the last decade have attracted the interest of the scientific community on this route of transmission, particularly in human immuno-deficiency virus (HIV)-infected individuals<sup>[37]</sup>. Perinatal transmission of HCV infection from HCV-monoinfected mothers occurs infrequently (around 3% of the cases), whereas it reaches 20% among HIV-coinfected mothers [38]. Other risk factors for the acquisition of HCV infection have been described, including acupuncture, tattooing, body piercing, some cosmetic procedures, sharing of shaving razors, nail scissors and other personal effects, and needle-stick injury for healthcare workers<sup>[28]</sup>.

# MODES OF EXPOSURE AND FACTORS ASSOCIATED WITH HBV AND HCV TRANSMISSION IN HEALTHCARE WORKERS

Healthcare workers are exposed to human blood and other potentially infectious biological material more frequently than the general population. Among the 60 or more agents responsible for blood-borne transmissible infectious diseases, HCV and HBV are those most frequently transmitted to healthcare workers. Contact with potentially infectious material occurs in most cases through mucosal-cutaneous or percutaneous exposure. In mucosal-cutaneous exposure, a patient's blood, blood derivative or other potentially infected biological material accidentally enters into contact with the mucous membranes of the eyes or mouth or with the skin, healthy or non-intact, of a healthcare worker<sup>[39]</sup>. Percutaneous exposure occurs when an operator receives an injury with a sharp contaminated object, such as a needle, blade or piece of glass. Around 75% of the total occupational exposure is percutaneous and the remaining 25% mucosal-cutaneous. The risk of HBV or HCV infecting a healthcare worker is higher in percutaneous than in mucosal-cutaneous exposure. The rate of transmission of HCV infection can be five times higher in percutaneous than in mucosal-cutaneous exposure, but the risk of acquiring these infections through conjunctival exposure is also high.

A prominent role in the transmission of an infection



is also played by the degree of infectiveness of the contaminated biological material to which the healthcare worker has been exposed<sup>[40-42]</sup>. The highest rates of transmission of HBV or HCV infection follow exposure to blood or its products, but transmission can also occur, generally at a lower rate, after exposure to ascites, cerebrospinal fluid or solutions from cell cultures. HBV and HCV transmissions have never been observed following exposureto feces, urine, sweat, vomitor tears.

Other main factors significantly affecting the likelihood of transmission of infecting agents are the extent and depth of the cutaneous or mucosal wound and the volume of blood transferred<sup>[40-43]</sup>. All punctures from contaminated needles and sharp objects may be responsible for the transmission of infections. However, the medical devices used to access the blood vessels directly cause most of the conversions to positivity of HCV and HBV serum markers worldwide. Such conversions are less frequent after the intramuscular or subcutaneous use of hollow needles or the use of lancets for capillary blood collection, due to the lesser amount of organic material present on their surface. Nurses generally perform these clinical practices and are the occupational group with the highest risk of needle-stick injuries[40-43].

The risk of exposure is also related to the medical procedure performed. For example, of the 99 percutaneous injuries observed by Tokars *et al*<sup>[44]</sup> during 1382 surgical operations in five different wards (general, orthopedic, gynecologic, traumatic and cardiac surgery), most (73%) were related with the suturing. Risk factors for percutaneous injuries included the performing an emergency procedure, a patient blood loss greater than 250 mL, and a duration of surgery procedure greater than 1 h<sup>[45]</sup>.

The HBV load in the source patient may influence the risk of transmission of HBV infection to non-immune healthcare workers. In these cases, the risk of HBV transmission is estimated at 19%-30%, if the source patient is HBeAg-positive or shows an HBV load > 10<sup>6</sup> IU/mL and at 5% if the source patient is HBeAg-negative or has a lower HBV load. The anti HBV vaccination of healthcare workers was introduced in the 1980s in most countries, but a substantial number of healthcare workers worldwide have eluded vaccination and, despite the excellent immunogenicity of the vaccine, about 20% of vaccinated subjects show anti-HBs titers lower than 10 IU/mL. It is common opinion, however, that HBVvaccinated subjects with an anti-HBs titer below 10 IU/mL and those who have become anti-HBs-negative can be considered protected against HBV infection, since the immunological memory for HBsAg may persist even in these cases and ensure a rapid rise in protective antibodies in the case of an HBV assault [46-48]. Nevertheless, a highly infectious HBV inoculum might overpower a low antibody titers against HBsAg (anti-HBs) titer during the long professional life of a healthcare worker. In these cases, the administration of a booster dose of HBV vaccine could be considered<sup>[49]</sup>.

The transmission of HCV infection occurs in nearly 10% of the healthcare workers after parenteral exposure to the blood of an HCV-RNA-positive source patient, a rate that may vary according to the HCV load of the source patient<sup>[39,42]</sup>.

#### PRE-EXPOSURE MANAGEMENT

The prevention of exposure remains the primary strategy for reducing occupational infections by blood-borne pathogens. The healthcare organizations should make available for their personnel a system that includes written protocols for prompt reporting, evaluation, counseling, treatment, and follow-up of occupational exposures<sup>[39]</sup>. Healthcare workers should be trained to adopt effective measures to prevent infections from occupational exposure to blood, *i.e.*, eliminating unnecessary injections, implementing universal precautions, eliminating needle recapping and disposing of the sharp into a sharps container immediately after use, use of safer devices such as needles that sheath or retract after use<sup>[50]</sup>.

Furthermore, healthcare workers should be aware that any person at risk of contact with blood, blood-contaminated body fluids, other body fluids, or sharps should be vaccinated against HBV<sup>[51]</sup>. The vaccination should happen early after the start of their career to avoid infection and development of carrier status. The healthcare workers should be vaccinated with a standard vaccination schedule and the serum anti-HBs should be assessed 1-2 mo after completion of a 3-dose vaccination series<sup>[52]</sup>. The HBV vaccination is, therefore, an essential part of prevention and control of HBV infection for healthcare workers and its use was one of the causes of drastic reduction of its prevalence in healthcare workers.

#### POST-EXPOSURE MANAGEMENT

Although the primary prevention constitutes the first line of defense against the risk of occupational infections by blood-borne viruses, the adequate management of exposures with the post-exposure prophylaxis constitutes a key element in managing and limiting the transmission of these infections to staff exposed.

Regarding HBV infection, the risk of infection and the post-exposure management depends on the HBV status of the source and of the healthcare worker.

The risk of developing clinical hepatitis or serological evidence of HBV infection is high (22%-31% and 37%-62%, respectively) if the source is HBsAg and HBeAg positive, and low (1%-6% and 23%-37%, respectively) if it is HBsAg positive and HBeAg negative<sup>[28]</sup>. Moreover, it needs to evaluate the serological status of the healthcare worker: If HBsAg, anti-HBs (or titer less than 10 IU/mL) and HBV core antigen (anti-HBc) are negative, the healthcare worker is at risk to HBV infection. Precisely, in this case it should be taken in account the post exposure prophylaxis with a first dose of HBV vaccine and anti-HBV-specific immunoglobulin



Table 1 Prevalence of hepatitis B virus infection in healthcare workers

Ref.	Year of enrollment	Country	No. of subjects	Type of study	HBsAg positive, n (%)	Anti-HBc positive, n (%)
Elzouki et al <sup>[54]</sup>	2008	Libya	601	Cross-sectional	11 (1.8)	51 (8.5)
Alqahtani et al <sup>[55]</sup>	NR	Saudi Arabia	300	Cross-sectional	1 (0.3)	25 (8)
Arguillas et al <sup>[56]</sup>	1990	Philippines	123	Case-control	8 (6.5)	81 (65.8)
Aziz et al <sup>[57]</sup>	NR	Pakistan	250	Cross-sectional	6 (2.4)	
Butsashvili <i>et al</i> <sup>[58]</sup>	2006	Georgia	1386	Cross-sectional	28 (2)	402 (29)
Fisker et al <sup>[59]</sup>	1998	Denmark	960	Cross-sectional	14 (1.5)	
Fritzsche <i>et al</i> <sup>[60]</sup>	2011	Cameroon	237	Cross-sectional	15 (6.3)	174 (73.4)
Kateera et al <sup>[61]</sup>	2013	Rwanda	378	Cross-sectional	11 (2.9)	
Kondili <i>et al</i> <sup>[62]</sup>	2004	Albania	480	Cross-sectional	39 (8.1)	338 (70)
Calleja-Panero et al <sup>[63]</sup>	2007-2010	Spain	4986	Cross sectional	36 (0.77)	
Ozsoy et al <sup>[64]</sup>	1998	Turkey	702	Case-control	21 (3)	
Petrosillo et al <sup>[65]</sup>	1985	Italy	5813	Cross-sectional	108 (1.8)	
Rehman et al <sup>[66]</sup>	1996	Pakistan	95	Case-control	5 (5)	27 (28)
Rybacki et al <sup>[67]</sup>	2009	Poland	520	Cross-sectional	6 (1.2)	99 (19)
Sarwar et al <sup>[68]</sup>	2006	Pakistan	125	Cross-sectional	3 (2.4)	
Slusarczyk et al <sup>[69]</sup>	2008	Poland	961	Cross-sectional	$4 (0.4)^1$	151 (15.7)
Thomas et al <sup>[70]</sup>	1991	United States	943	Case-control	1 (0.1)	59 (6.2)
Ciorlia et al <sup>[71]</sup>	1994-1999	Brazil	1433	Cross-sectional	11 (0.8)	

<sup>&</sup>lt;sup>1</sup>Hepatitis B virus-DNA positivity in anti-HBc-positive subjects. NR: Not reported; HBsAg: Hepatitis B surface antigen; Anti-HBc: Hepatitis B virus core antigen.

(HBIG), that should be initiated as soon as possible, preferably within 24 h of exposure and not more than 7 d. If the healthcare worker is vaccinated with protective antibody response ( $\geq$  10 IU/mL) or is anti-HBc positive, no treatment is needed.

Currently, there is no prophylaxis for HCV infection: In fact, immunoglobulin and antivirals are not recommended and only the observation is indicated. However, recently the available of the second and third wave direct antiviral agents enhanced the efficacy and tolerability of anti-HCV treatment<sup>[53]</sup>; consequently, the traditional management of HCV infection after exposure in healthcare workers probably should be revised.

### STUDIES ON HBV INFECTION IN HEALTHCARE WORKERS

The rates of HBsAg and anti-HBc positivity in healthcare workers reported in several studies published in the last three decades<sup>[54-70]</sup> range from 0.1% to 8.1% and from 6.2% to 73.4%, respectively, depending on the age of the subjects investigated, the spread of HBV infection in their country of origin and on the prevention strategies used by the healthcare workers (Table 1).

Of 5813 healthcare workers tested in Italy in 1985, 21.5% were found to be anti-HBc-positive and 1.8% HBsAg-positive [65]. A logistic regression analysis showed that the exposure to HBV infection was associated with male sex, an older age, history of blood transfusion, dental treatment, needle-stick injury and working in a healthcare setting (surgeons and nurses vs others). A similar rate of HBsAg positivity (1.5%) was observed in a study on 960 healthcare workers tested in Denmark in 1998<sup>[59]</sup>. A much higher HBsAg prevalence (8.1%) was detected in 480 healthcare workers investigated by Kondili et al<sup>[62]</sup> in 2004 in Albania, in accordance

with the widespread of HBV infection in this country. In this study, the highest rates of HBsAg positivity were found in the youngest age group (11.4% in the aged 20-30) and in the auxiliaries (12.6%), but a high HBsAg prevalence (7.2%-7.5%) was also found in the healthcare workers aged over 30. The anti-HBc seroprevalence was also extremely high (70%) in this study and was associated with an age over 40 (OR = 2.9; 95%CI: 1.9-4.6).

In a study performed in Lybia in 2008 on 601 health-care workers, the rate of HBsAg positivity was 1.8%, higher in nurses (2.3%) and lower in physicians (0.7%) and laboratory staff (0.8%)<sup>[54]</sup>. Of 237 healthcare workers tested in Cameroon, 6.3% were HBsAg-positive and 73.4% anti-HBc-positive, in accordance with the wide spread of HBV infection in this geographical area<sup>[60]</sup>. Seroprevalence studies conducted in Asia showed varying results. Aziz et  $a^{[57]}$ , Rehman et  $a^{[66]}$  and Sarwar et  $a^{[68]}$ , in three different studies conducted in Pakistan, reported that 2.4%, 5% and 2.4% of the healthcare workers, respectively, were HBsAg-positive.

Low rates of HBsAg positivity were found in two seroprevalence studies conducted on healthcare workers in the United States (0.1%) and Brazil (0.8%) $^{[63,70]}$ .

Some case-control studies allowing a comparison of the HBsAg prevalence in the healthcare workers with that of the general population provided contrasting results. Rehman *et al*<sup>[66]</sup>, in a small case-control study performed in Pakistan, enrolled 95 healthcare workers and 91 volunteer blood donors as controls and observed higher rates of HBsAg (14% *vs* 5%) and anti-HBc (36% *vs* 28%) positivity in the control group. Instead, in a case-control study conducted in Turkey<sup>[64]</sup>, the rate of HBsAg positivity was similar in 702 healthcare workers and 5670 blood donors (3% *vs* 2.1%), and in the Philippines, Arguillas *et al*<sup>[56]</sup> found 6.5% of 123 healthcare workers and 2.2% of 382 blood donors to be



Table 2 Prevalence of hepatitis C virus infection in healthcare workers

Ref.	Year of enrollment	Country	No. of patients	Type of study	Anti-HCV positive, n (%)
Elzouki et al <sup>[54]</sup>	2008	Libya	601	Cross-sectional	12 (2)
Alqahtani <i>et al</i> <sup>[55]</sup>	NR	Saudi Arabia	300	Cross-sectional	0
Arguillas et al <sup>[56]</sup>	1990	Philippines	123	Case-control	12 (9.7)
Aziz et al <sup>[57]</sup>	NR	Pakistan	250	Cross-sectional	14 (5.6)
Butsashvili et al <sup>[58]</sup>	2006	Georgia	1386	Cross-sectional	69 (5)
Fisker et al <sup>[59]</sup>	1998	Denmark	960	Cross-sectional	2 (0.14)
Fritzsche et al <sup>[60]</sup>	2011	Cameroon	237	Cross-sectional	4 (1.7)
Kateera et al <sup>[61]</sup>	2013	Rwanda	378	Cross-sectional	5 (1.3)
Kondili et al <sup>[62]</sup>	2004	Albania	480	Cross-sectional	3 (0.6)
Calleja-Panero et al <sup>[63]</sup>	2007-2010	Spain	4981	Cross sectional	31 (0.62)
Ozsoy et al <sup>[64]</sup>	1998	Turkey	702	Case-control	2 (0.3)
Petrosillo et al <sup>[65]</sup>	1985	Italy	5813	Cross-sectional	117 (2)
Rehman et al <sup>[66]</sup>	1996	Pakistan	95	Case-control	4 (4)
Rybacki et al <sup>[67]</sup>	2009	Poland	520	Cross-sectional	4 (0.8)
Sarwar et al <sup>[68]</sup>	2006	Pakistan	125	Cross-sectional	4 (3.2)
Slusarczyk et al <sup>[69]</sup>	2008	Poland	961	Cross-sectional	16 (1.7)
Thomas et al <sup>[70]</sup>	1991	United States	943	Case-control	7 (0.7)
Campello et al <sup>[72]</sup>	1990	Italy	407	Case-control	5 (1.2)
Zaaijer et al <sup>[73]</sup>	2000-2009	Denmark	729	Cross-sectional	1 (0.14)
Okasha et al <sup>[74]</sup>	2008	Egypt	1770	Cross-sectional	141 (8.0)

NR: Not reported; HCV: Hepatitis C virus.

HBsAg-positive. Finally, in the United States, Thomas et  $al^{70}$  observed the same HBsAg-positivity rate (0.1%) in 943 healthcare workers and 104239 blood donors, whereas they found a higher rate of anti-HBc positivity in the healthcare workers, 6.2% vs 1.8%, indicating a greater exposure to HBV in these subjects, but exposure was not followed by a chronic infection, most probably because it occurred in adulthood.

## STUDIES ON HCV INFECTION IN HEALTHCARE WORKERS

The prevalence of anti-HCV positivity in healthcare workers<sup>[54-74]</sup> ranges from 0% to 9.7% in different studies worldwide: 9.7% in the Philippines, 8% in Egypt, 3.2%-5.6% in three studies in Pakistan, 5% in Georgia, 0.14% in Denmark, 0.8% in Poland, 0.7% in the United States, 0.6% in Albania and 0.3% in Turkey (Table 2).

The majority of 1386 healthcare workers investigated in Georgia in 2006<sup>[58]</sup> stated an episode of occupational exposure to HCV infection, including accidental needlestick injuries in 45% of cases, cuts with contaminated instruments in 38% and blood splashes in 46%. For the healthcare workers who received a cut, this unfavorable event occurred during the reassembling of tools or when receiving tools from a colleague in the majority of the cases, and the highest proportion of needle-stick injuries occurred when recapping used needles, more frequently in nurses (39%) than in physicians (22%).

In a cross-sectional study performed on 1770 health-care workers in Egypt in 2008<sup>[74]</sup>, the anti-HCV seroprevalence was 8.0%, the estimated incidence of HCV infection 7.3 per 1000 persons-year and the risk factors independently associated with HCV seropositivity were an older age, performing a manual job, having a history

of blood transfusion or a history of parenteral treatment for schistosomiasis.

Only five case-control studies compared the prevalence of HCV infection in healthcare workers and in the general population of the same country<sup>[56,64,66,70,72]</sup>. Four of these 5 studies showed similar prevalences of anti-HCV positivity in the two groups of subjects: 0.3% vs 0.4%, respectively, in a study from Turkey on 702 healthcare workers  $^{\rm [64]}$  and 5670 blood donors, 1.6% in 123 healthcare workers and 2.2% in 382 blood donors investigated in the Philippines<sup>[56]</sup>, 1.2% in 407 healthcare workers and 0.8% in pregnant women studied in Italy<sup>[72]</sup> and 0.7% in 943 healthcare workers and 0.4% in 104239 blood donors in the United States<sup>[70]</sup>. Unexpectedly, but similarly to what was observed for HBsAg by Rehman et al<sup>[66]</sup> in a study in Pakistan (see above), they observed that the 95 healthcare workers less frequently than the 91 blood donors were anti-HCV positive (4% vs 14%). The results of this study are of difficult interpretation.

#### **CONCLUSION**

Mucosal-cutaneous and percutaneous exposure to human blood or bloodstained medical instruments occurs more frequently in healthcare workers than the general population. A major role in the transmission of HBV or HCV infection is played by the virus concentration on the infecting materials, high in blood and blood products, much lower in ascites and in cerebrospinal fluid and at non-infectious concentrations in feces, urine, sweat, vomit and tears.

The characteristics of the wound received by a healthcare worker and the volume of blood transferred are other main factors influencing a possible transmission of HBV or HCV infection. In fact, the devices



used to access the blood vessels directly, more frequently than cable needles used for intramuscular or subcutaneous treatments, are responsible for HBV and HCV transmission because of the higher amount of organic material carried on their surface.

The transmission of HBV infection from a source patient to a healthcare worker is also influenced by the natural or vaccine-induced immunological protection against HBV in the healthcare worker. Although HBV vaccination of anti-HBs-negative healthcare workers is highly recommended in all countries, some healthcare workers have eluded vaccination and some were low-or non-responders to the vaccine, indicating that a highly infectious HBV inoculum might overpower low immunological protection.

Since no anti-HCV vaccine is at present available to counteract HCV transmission, healthcare workers should protect themselves by meticulously applying all the universal prophylactic measures whenever potentially exposed.

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