

Original Article

## HBV and HCV serological monitoring among injection drugs users in opiate substitution treatment in Bosnia and Herzegovina

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### Abstract

**Introduction:** Use of intravenous heroin carries a risk of serious medical conditions, including acquiring blood-borne infections. Therefore, hepatitis B virus (HBV) and hepatitis C virus (HCV) infection represent a threat for people who inject drugs (PWID). The objectives of this study were to determine the extent and characteristics of risk factors for acquiring HBV and HCV infection in PWID included in opiate substitution treatment in the southern part of Bosnia and Herzegovina (B&H).

**Methodology:** The study included 120 adult PWID of both sexes who participated in opiate substitution treatment. All participants were interviewed, and their blood samples were tested for the presence of the surface hepatitis B virus antigen (HBsAg) and hepatitis C virus antibodies (anti-HCV). Prevalence data were obtained and compared to the serological status.

**Results:** HBsAg prevalence among PWID was 0.8% (1/120), whereas seroprevalence of anti-HCV was 52.5% (63/120). PWID exposed to risk-behavior factors (such as unsafe sexual activity, serving prison sentence, and tattooing) were more frequently anti-HCV positive. Sharing drug paraphernalia was found to be the most significant risk factor. The highest predictive values for acquiring HCV-infection were attributed to PWID who used heroin for more than three years and who were unmarried.

**Conclusions:** HBsAg prevalence among PWID is rare (0.8%), while HCV-infection (52.5%) presents an important health and social issue among PWID in B&H. Sharing drug paraphernalia and intravenous heroin use longer than three years were the most prominent risk-behavior factors among the patients we investigated.

**Key words:** prevalence; risk factors; hepatitis B virus; hepatitis C virus; drug users; opiate substitution treatment.

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### Introduction

According to estimates from 2004, two billion people, constituting one-third of the world's population, have been infected with hepatitis B virus (HBV), while 350 million people have a chronic infection [1]. Around 80 (64–103) million people worldwide are infected with hepatitis C virus (HCV). Previous estimates were that every year, three to four million people become infected with HCV [2,3].

According to the latest United Nations Office on Drugs and Crime reports, around 16.5 million people (0.4% of the total world population) 15 to 64 years of age use heroin or opium [4]. The characteristics of the virus and the very method of injecting the drug make this particular route of drug administration the most significant risk factor for spreading of HBV and HCV,

even more than spreading of human immunodeficiency virus (HIV). Among people who inject drugs (PWID), the prevalence of surface hepatitis B virus antigen (HBsAg) carriers ranges from 5% to 10% across 21 countries, while in 10 countries it exceeds 10%. In 26 countries, there is a 60% to 80% prevalence of antibodies for hepatitis C virus (anti-HCV) in PWID, while in 12 countries it exceeds 80%. In total, it is estimated that about 1.2 million (0.3–2.7 million) PWID might be anti-HCV positive and 10.0 million (6.0–15.2 million) HBsAg positive [5].

As a developing country, Bosnia and Herzegovina (B&H) does not have a strong public health system. At present, there are no accurate data on the number of PWID in B&H since the overall data of the 2013 census have not yet been published. Therefore, the unofficial

estimates place the number of PWID in B&H at 12,228 (9,213–15,243) according to studies conducted in 2012, whereas the prevalence of HBV and HCV infection is estimated to be as high as 5.5% and between 12% and 43%, respectively [6].

HBV vaccination has generally been provided through a statutory national vaccination program for newborns since 2001. Unfortunately, the majority of PWID have not been vaccinated against HBV since there were no targeted vaccination programs for the most-at-risk population (PWID, sex workers, men who have sex with men).

Needle and syringe programs are available outside prisons. Despite the low coverage of access for PWID to clean syringes through specialized programs, studies have shown relatively high percentages of injecting drug users using sterile equipment in their last injection, which suggests that the sterile injecting equipment may be available outside the specialized services [6].

The aim of the study was to determine the prevalence of HBV and HCV infections among PWID who received opiate substitution treatment (OST) in the southern areas of B&H. Different characteristics of

drug use and risk factors were compared among HCV-seropositive and HCV-seronegative PWID.

**Methodology**

The study was done on a randomly selected sample of 120 adult PWID of both sexes who were not different by gender and age in relation to 177 total PWID included in a treatment program at the only regional OST center. Patients were divided into two subgroups (HCV seropositive or HCV seronegative). The interview was conducted by applying a questionnaire compiled for this purpose (modified Pompidou questionnaire), which contained general, demographic, social, and health variables relevant to the study. Blood samples were taken from patients by venipuncture, were coded and centrifuged, and blood sera were tested for the presence of HBsAg and anti-HCV by enzyme-linked immunosorbent assay (ELISA) (Architect System i2000 device, Abbott Laboratories, Abbott Park, USA) in the laboratory of the University Hospital Mostar. Prior to the in-depth interviews, verbal informed consent/assent was obtained from each patient. The protocol was conducted in accordance with

**Table 1.** Risk-behavior factors among people who inject drugs (PWID) in relation to hepatitis C virus (HCV) status.

Variables	Anti-HCV– n (%)	Anti-HCV+ n (%)	$\chi^2$	p	RR	95% CI
<b>Sharing drug paraphernalia</b>			11.245	0.001	1.917	1.248–2.944
Yes	14 (40.0)	46 (76.7)				
No	21 (61.0)	14 (23.3)				
<b>Sexual orientation</b>			< 0.001†	0.615	1.810	0.169–19.426
Bisexual	1 (1.8)	2 (3.2)				
Heterosexual	56 (98.2)	61 (96.8)				
<b>Regular use of condoms</b>			0.147	0.701	1.092	0.806–1.478
Yes	25 (43.9)	24 (38.7)				
No	32 (56.1)	38 (61.3)				
<b>Unprotected sex with addict</b>			3.338	0.066	1.640	1.000–2.688
Yes	16 (28.1)	29 (46.0)				
No	41 (71.9)	34 (54.0)				
<b>Transfusion</b>			0.620	0.431	0.622	0.254–1.525
Yes	10 (17.9)	7 (11.1)				
No	46 (82.1)	56 (88.9)				
<b>Serving prison sentence</b>			0.625	0.429	1.301	0.767–2.205
Yes	16 (28.1)	23 (36.5)				
No	41 (71.9)	40 (63.5)				
<b>Acupuncture</b>			0.008†	0.604	0.452	0.042–4.857
Yes	2 (3.5)	1 (1.6)				
No	55 (96.5)	62 (98.4)				
<b>Tattooing</b>			1.439	0.230	1.237	0.911–1.678
Yes	30 (52.6)	41 (65.1)				
No	27 (47.4)	22 (34.9)				
<b>Piercing</b>			0.652	0.419	0.517	0.160–1.674
Yes	7 (12.3)	4 (6.3)				
No	50 (87.7)	59 (93.7)				

†Fisher’s exact test.

the Declaration of Helsinki, B&H law on health care, and law on rights, obligations, and responsibilities of patients. The research was approved by the ethics committee at the University Hospital Mostar (No 2514/11).

For statistical analysis, the Windows-based SPSS program version 13 was used (IBM, Armonk, USA). Data were presented as frequency (n) and percentage (%) for nominal variables, and as mean (M) and standard deviation (SD) for continuous variables. Differences between nominal variables were tested by the Chi-square test. For relationships between nominal variables, relative risks (RR) with confidence intervals (95% CI) were calculated. Logistic regression analysis was used for independent predictive values of risk factors for acquiring HCV infection among PWID. Results are presented as odds ratio (OR) and 95% CI. Statistical significance was set at  $p < 0.05$ .

## Results

Out of the total number of PWID, only one was HBsAg positive (0.8%), and this patient was also anti-HCV positive. The prevalence of anti-HCV among PWID was 52.5% (63/120).

Anti-HCV-positive PWID shared drug paraphernalia considerably more often (RR: 1.917;

95% CI: 1.248–2.944) than did the anti-HCV-negative PWID. Risk factors such as sexual orientation (RR: 1.810; 95% CI: 0.169–19.426), regular condom use (RR: 1.092; 95% CI: 0.806–1.478), unsafe sexual activity with male or female addicts (RR: 1.640; 95% CI: 1.000–2.688), blood and blood product transfusion (RR: 0.622; 95% CI: 0.254–1.525), having served a prison sentence (RR: 1.301; 95% CI: 0.767–2.205), acupuncture (RR: 0.452; 95% CI: 0.042–4.857), tattooing (RR: 1.237; 95% CI: 0.911–1.678), and piercing (RR: 0.517; 95% CI: 0.160–1.674) did not vary significantly between groups in relation to serological HCV status (Table 1). Intravenous administration (52.4%;  $p < 0.001$ ) and use of intravenous drugs for longer than three years (71.2%;  $p < 0.001$ , Fisher's exact test) were statistically more frequent among anti-HCV positive PWID than among anti-HCV-negative PWID. Secondary drugs and the frequency of intravenous administration were similarly present (Table 2).

The highest predictive value for acquiring HCV-infection was found among PWID practicing intravenous heroin administration for longer than three years (OR: 11.691; 95% CI: 3.255–41.993), followed by those with unmarried status (OR: 7.128; 95% CI: 1.410–36.034) and earlier age of the first use of

**Table 2.** Different characteristics of drug use among people who inject drugs (PWID) in relation to hepatitis C virus (HCV) status.

Variables	Anti-HCV <sup>-</sup> n (%)	Anti-HCV <sup>+</sup> n (%)	$\chi^2$	p
<b>Secondary drug</b>			1.600 <sup>†</sup>	0.856
Cocaine	9 (17.3)	7 (11.9)		
Amphetamines	1 (1.9)	2 (3.4)		
Ecstasy	3 (5.8)	2 (3.4)		
Benzodiazepines	4 (7.7)	4 (6.8)		
Cannabinoids	35 (67.3)	44 (74.6)		
<b>Principal administration method</b>			21.809	< 0.001
Intravenous	7 (12.3)	33 (52.4)		
Smoking	24 (42.1)	13 (20.6)		
Insufflations	26 (45.6)	17 (27.0)		
<b>Duration of IV use</b>			18.144 <sup>†</sup>	< 0.001
Up to 1 month	6 (23.1)	2 (3.4)		
2–6 months	5 (19.2)	4 (6.8)		
7–12 months	2 (7.7)	1 (1.7)		
1–3 years	6 (23.1)	10 (16.9)		
More than 3 years	7 (26.9)	42 (71.2)		
<b>Frequency of IV use</b>			1.599 <sup>†</sup>	0.973
1–5 times total	3 (5.5)	5 (7.9)		
1–3 times a month	9 (16.4)	9 (14.3)		
Once a week	2 (3.6)	3 (4.8)		
2–6 days in a week	1 (1.8)	3 (4.8)		
Every day	5 (9.1)	5 (7.9)		
Irregular	6 (10.9)	8 (12.7)		
Did not use previous month	29 (52.7)	30 (47.6)		

<sup>†</sup>Fisher's exact test.

**Table 3.** Predictive values of risk factors for acquiring hepatitis C virus (HCV) infection among people who inject drugs (PWID).

Variable	HCV infection				
	B	SE	Wald	p	OR (95% CI)
Intravenous heroin use > 3 years	2.459	0.652	3.769	< 0.001	11.691 (3.255–41.993)
Unmarried	1.964	0.827	2.376	0.018	7.128 (1.410–36.034)
Age of first reporting for addiction treatment	-0.097	0.049	1.994	0.046	0.908 (0.826–0.998)

B: regression coefficient; SE: standard error.

intravenous drugs (OR: 0.908; 95% CI: 0.826–0.998) (Table 3).

**Discussion**

Our study shows that individually observed chronic HBV infection prevalence measured by the presence of HBsAg is significantly lower compared to the world average. Lower immunity due to poorer health and other viral infections, as well as repeated exposure (size of inoculum and duration of exposure), should increase the number of chronically infected PWID [7]. Of note is that among anti-HCV-positive PWID, only 8/120 (6.7%) were vaccinated against HBV, whereas 112/120 of them (93.3%) were neither vaccinated nor were aware of the possibility of vaccination against HBV. In the anti-HCV-negative group, 4 (7.0%) subjects had been previously vaccinated against HBV, whereas 53 (93.0%) received no such vaccination. The possible explanation for the low prevalence of HBsAg presence among PWID could be due to fact that chronic HBV-infection prevalence among the general population in B&H is still relatively low, but the suppressive effect of HCV on HBsAg expression should also be taken into consideration [8]. It is important to point out that the detection of HBsAg in PWID is not completely reliable evidence of infection; a study of the anti-HBc antibodies would provide more accurate data on the prevalence of HBV in PWID. Unfortunately, due to limited resources, such a study remains a goal of future research.

Additionally, the rate of HCV seroprevalence (52.5%; 63/120) among PWID is also lower than it is in many European countries and in the world, where it ranges from 60% to 80% among PWID in 26 countries, and exceeds 80% in 12 countries [5]. The results of the study show that the seroprevalence of HCV infection is similar to that in neighboring countries (Croatia, 40.5%; Serbia, 69%; and Montenegro, 60%), possibly due to the poor social and economic situation in the region [9-11]. Although anti-HCV may indicate an acute, chronic, or resolved HCV infection, a well-known high degree of chronicity of HCV allows us to be confident that measuring anti-HCV is a sufficiently reliable epidemiological indicator of the presence of HCV

infection (*i.e.*, contact with HCV). At the time of this study, PWID were not allowed to participate in treatment of HCV infection in the public health system, and there were no privately funded programs of treatment with interferon.

Although risk-behavior factors in relation to HCV status are more or less the same among PWID globally, our findings suggest certain local particularities, which have led us to conclude that aside from sharing drug paraphernalia, other risk factors such as transfusion, acupuncture and piercing, serving a prison sentence, as well as sexual orientation and regular condom use, do not play a significant role among the investigated PWID in B&H [12,13].

Cannabinoids are recognized as the main secondary drug among PWID regardless of their serological status, which is not surprising considering its low price, widespread availability, and trend of using cannabinoids in Europe [14]. A similar relationship between heroin administration method and prevalence of anti-HCV has been noted in comparable studies conducted in the United States [15]. Intravenous heroin use for longer than three years showed the highest predictive value for acquiring HCV infection, which corresponds with the results of similar studies conducted in Hong Kong and Brazil [16,12].

Overall, given the difficulties encountered by the PWID community (stigmatization, lack of understanding from their social environment, and unavailability of healthcare system), it would also be interesting to explore other characteristics of hepatotropic viral infections (hepatitis A, D and E, as well as Epstein–Barr virus and cytomegalovirus) in PWID. This primarily includes molecular techniques such as polymerase chain reaction (PCR) and detection of virus subtypes, which would, in effect, have professional and prognostic significance for treatment, allowing more accurate estimates of acute, chronic, or resolved infection as well as immunity.

**Conclusions**

The data obtained in this study represent the first scientifically proven records of the HBV and HCV infections among PWID in B&H, which is important

since adequately conducted studies in B&H and low-income countries are lacking. Moreover, HCV infection is a very important health and social issue among PWID, and these data may be helpful for creating national or international plans for prevention, control, treatment, or possible elimination of HBV/HCV infection, regardless of patient- and system-related barriers.

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