

Continued high prevalence of HIV, HBV and HCV among injecting and noninjecting drug users in Italy

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Summary. We estimated the prevalence of HIV, HBV and HCV infections among injecting and non-injecting drug users treated within public drug-treatment centres in Italy to determine the correlates of infection. In the sample of 1330 drug users, the prevalence of HIV was 14.4% among drug injectors and 1.6% among non-injectors; the prevalence of HBV was 70.4% among injecting drug users and 22.8% among non-injectors and of HCV was 83.2% among injecting drug users and 22.0% among non-injectors. Old age, unemployment, and intravenous drug use were significantly correlated with each of the infections, as well as a longer history of injecting drug use. The results indicate that these infections continue to circulate among drug users, highlighting the need for monitoring of this group in Italy.

Key words: HIV, hepatitis B, hepatitis C, drug users.

Riassunto (*Alta prevalenza di HIV, HBV e HCV tra i tossicodipendenti iniettivi e non iniettivi in trattamento presso i SerT italiani*). Abbiamo stimato la prevalenza dell'infezione da HIV, HBV e HCV tra i tossicodipendenti iniettivi e non iniettivi che sono in trattamento presso i Servizi Pubblici per le Farmacodipendenze e l'Alcolismo italiani (SerT) e abbiamo determinato i correlati per queste infezioni. Tra i 1330 tossicodipendenti, la prevalenza dell'HIV era del 14,4% tra gli iniettivi e del 1,6% tra i non iniettivi; dell'HBV era del 70,4% tra gli iniettivi e del 22,8% tra i non iniettivi e dell'HCV era del 83,2% tra gli iniettivi e del 22,0% tra i non iniettivi. L'età avanzata, l'essere disoccupato e l'uso iniettivo sono risultati essere fattori significativamente associati con queste infezioni, così come una lunga storia di uso iniettivo tra gli endovenosi. Lo studio sottolinea la necessità di una sorveglianza continua di queste infezioni nella popolazione tossicodipendente.

Parole chiave: HIV, epatite B, epatite C, consumatori di droghe.

INTRODUCTION

In Italy, the proportion of AIDS cases represented by injecting drug users (IDU) has decreased [1]. However, injecting drug use is still an important modality of exposure not only to HIV but also to other blood borne infections. According to data from the Italian Surveillance System of acute viral hepatitis ("SEIEVA"), between 1997-2004, 13% of the cases of acute infection with hepatitis B virus (HBV) were attributable to injecting drug use, although in 2005 they decreased to 5% [2]. Injecting drug use was also the main risk factor for acute HCV infections until 2000, and afterwards it remained one of the three main risk factors (in 2005, IDUs represented 36.0% of the cases) [2].

In Italy, data on the seroprevalence of HIV, HBV and HCV infections among drug users are only avail-

able from public drug treatment centres ("SerT") [3]. The data refer to approximately half of the SerTs patients due primarily to the lack of specific national guidelines on serologic testing which do not make mandatory testing in SerT. Moreover, the data provided by SerTs are aggregated (and not individual) and thus cannot be correlated with socio-demographic information or with variables linked to drug abuse. Within this framework, in 2005 we conducted a cross-sectional study to estimate the prevalence of HIV, HBV, and HCV infections among SerT patients and to determine the correlates of infection.

MATERIALS AND METHODS

There are 550 SerTs located throughout Italy. SerTs offer free drug treatment, medical care and psycho-

logical assistance on an outpatient basis. Attendance is voluntary.

We selected the study sample by randomly choosing 30 patients from those attending SerTs in 2005, from each of 50 SerTs that were selected randomly, on the basis of probability proportional to size sampling (derived from the total number of drug users attending the SerTs annually). Forty-six (92%) of the SerT centres participated. Among the drug users selected, those who refused to participate were excluded. Fifty (3.6%) of the selected 1380 drug users refused to participate. Therefore, the total study population consisted of 1330 drug users.

After having provided written informed consent, the subjects underwent a structured interview using an anonymous questionnaire designed for this study and administered by SerT personnel. The questionnaire included socio-demographic data and information on sexual behaviour and drug use (including type of drug used and mode of administration). The SerT clinical records of each patient were reviewed to obtain information on the serological status for infections, in particular: HIV (HIVAb), HBV (HBsAg and HBcAb), and HCV (HCVAb). The serological tests for HIV, HBV, HCV had been performed with enzyme immune assays (EIA); positive EIA results for HIVAb were confirmed with a Western Blot assay and positive EIA results for HCVAb were confirmed with a recombinant immunoblot assay.

The prevalence of HIV infection was calculated by considering the proportion of drug users who were HIV positive among those who tested positive at any time plus those who tested negative in the 12 months before the interview. The same method was used to calculate the prevalence of HBV and HCV infections. Drug users who had not undergone testing for the above infections in the previous 12 months were excluded. Those who had not been tested were compared with those who had been tested and all the variables that were significantly associated with the HIV, HBV, and HCV testing were included in the multivariate model analysis as control variables.

For each infection, the seropositive and seronegative subjects were compared in terms of socio-demographic and behavioural characteristics, using the chi-square test. Variables were excluded if more than 5% of patients did not report data. In order to identify factors that correlated with infection, we built three multivariate logistic regression models, in which serological status was considered as the dependent variable. All other variables that in the univariate analysis had a p-value lower than 0.05 were considered as independent variables. Variables related to intravenous drug use (*i.e.*, number of years of injecting use and frequency of heroin injecting use) were not included in the multivariate model because they were only pertinent for the IDUs subgroup. The fitness of the final models was assessed with the likelihood ratio test. We did not perform

separate analyses for injecting and non-injecting users because there were very few non-injecting users tested ($n=184$ for HIV infection; 114 for HBV infection; and 214 for HCV infection). However, in the multivariate model, we entered "IDU" as a control variable, both because it was associated with testing and because it is known to be associated with these infections. IDUs were defined as those persons who injected at least once in their lifetime.

RESULTS

The sample consisted of 84% males (median age: 35 years; interquartile range: 28-40). The median time between first injection and the first visit at the SerT was 3 years (interquartile range: 1-8).

Thirty-four percent of the drug users had been attending the SerT for more than 10 years, and 65.0% were undergoing methadone treatment. The most commonly used substances were: heroin (93.2%), cannabis (63.5%), cocaine (62.3%), and alcohol (22.6%). Daily drug use in the six months prior to the SerT attendance was reported by 71.4% of heroin users and 44.8% of cannabis users. The use of more than one type of drug was very common: 83.5% of the drug users used two or more substances simultaneously. In the entire sample, 1009 (75.9%) injected at least one substance. Intravenous use was very common among both heroin users (80.2%) and cocaine users (45.4%). In the group of the heroin users, 56.9% had engaged in intravenous use for more than 10 years. In the whole sample, 67.5% had more than 5 sexual partners in their lifetime; the median age of the first sexual experience was 16 years (interquartile range: 15-18).

The HIV prevalence was 11.5% among the 807 (60.7%) drug users tested, 14.4% among the 533 IDUs, and 1.6% among the 181 non-injectors. Among IDUs, the probability of infection increased significantly with the number of years of injecting use. In the multivariate analysis, the socio-demographic correlates of HIV infection were: older age, geographical location of SerT, employment status and injecting use (at least once in a lifetime) (*Table 1*).

A total of 388 (29.2%) drug users who had already been vaccinated for HBV, were excluded from the calculation of the prevalence (vaccination status obtained from the SerT clinical records). The prevalence was calculated among the 563 drug users tested, who represented 59.8% of those who had not been vaccinated. The overall prevalence was 60.7% [82 (14.6%) positive for HBsAg and 260 (46.2%) for HBcAb]. Among the 449 IDUs, the prevalence was 70.4%, and the probability of infection increased with the number of years of injecting use. In fact, it was more than twice as high for IDUs who injected three or more times a week, as compared to those who injected up to twice a week. In the multivariate analysis, the correlates of HBV infection were: older age, being unemployed, injecting use and being HIV-positive (*Table 1*).

Table 1 | Prevalence and correlates for HIV, HBV and HCV infections among drug users attending public drug treatment centres in Italy, 2005

	Tested for HIV	HIV + N	(%)	Crude OR (95% CI)	Adjusted OR (95% CI)	Tested for HBV	HBV+ N	(%)	Crude OR (95% CI)	Adjusted OR (95% CI)	Tested for HCV	HCV+ N	(%)	Crude OR (95% CI)	Adjusted OR (95% CI)	
Total	807	93	(11.5)			563	342	(60.7)			1085	772	(71.2)			
Gender																
Male	648	70	(10.8)	1	1 (a)	465	271	(58.3)	1	1	890	636	(71.5)	1	1 (b)	
Female	156	23	(14.7)	1.43 (0.86-2.37)	1.61 (0.90-2.89)	94	67	(71.3)	1.77 (1.09-2.88)	1.66 (0.92-3.00)	190	132	(69.5)	0.90 (0.64-1.27)	1.09 (0.69-1.72)	
Age group																
< 31 years	283	7	(2.5)	1 (c)	1	136	48	(10.3)	1	1	339	169	(33.6)	1	1	
31-40 years	344	39	(11.3)	5.04 (2.22-11.46)	4.59 (1.94-10.83)	261	160	(61.3)	2.90 (1.89-4.47)	2.45 (1.51-4.11)	480	371	(77.3)	3.42 (2.53-4.62)	3.55 (2.38-5.29)	
> 40 years	180	47	(26.1)	13.93 (6.13-31.65)	11.17 (4.73-26.37)	166	134	(80.7)	7.68 (4.56-12.93)	5.83 (3.21-10.55)	266	232	(87.2)	6.86 (4.51-10.42)	6.58 (3.85-11.26)	
Area of SerT																
Central and Southern Italy	438	41	(9.4)	1	1	197	134	59.5%	1	1 (d)	625	444	(71.0)	1	1	
Northern Italy	369	52	(14.1)	1.59 (1.03-2.45)	1.67 (1.04-2.70)	145	87	62.5%	1.13 (0.80-1.60)	1.24 (0.80-1.92)	460	328	(71.3)	1.01 (0.77-1.32)	0.93 (0.66-1.32)	
Number of years of education																
< = 8 years	393	56	(14.2)	1	1	309	206	(66.7)	1	1	559	434	(77.6)	1	1	
> 8 years	409	37	(9.0)	0.59 (0.38-0.93)	0.76 (0.47-1.24)	253	135	(53.4)	0.57 (0.41-0.80)	0.69 (0.46-1.06)	520	333	(64.0)	0.51 (0.39-0.67)	0.59 (0.42-0.84)	
Employment status																
Employed	476	43	(9.0)	1	1	332	178	(53.6)	1	1	642	431	(67.1)	-	-	
Unemployed	324	49	(15.1)	1.79 (1.16-2.78)	1.85 (1.14-3.00)	225	158	(70.2)	2.04 (1.43-2.92)	2.10 (1.35-3.28)	432	211	(32.9)	-	-	
Marital status																
Single	463	44	(9.5)	1	1	315	183	(58.1)	-	-	613	417	(68.0)	1	1	
Married/divorced/separated	337	48	(14.2)	1.58 (1.02-2.44)	1.01 (0.62-1.65)	245	157	(64.1)			464	349	(75.2)	1.42 (1.08-1.87)	0.96 (0.66-1.39)	

(continued)

Table 1 | Continued.

	Tested for HIV	HIV + N	(%)	Crude OR (95% CI)	Adjusted OR (95% CI)	Tested for HBV	HBV+ N	(%)	Crude OR (95% CI)	Adjusted OR (95% CI)	Tested for HCV	HCV+ N	(%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Number of lifetime sexual partner															
< 5	235	29	(12.3)	-	-	167	85	(50.9)	1	1	329	220	(66.7)	1	1
> = 5	560	63	(11.3)	-	-	382	249	(65.2)	1.81 (1.25-2.61)	1.47 (0.93-2.31)	735	536	(72.9)	1.33 (1.01-1.77)	1.58 (0.80-1.68)
Injecting drug user (IDU)															
No	184	3	(1.6)	1	1	114	26	(22.8)	1	1	214	47	(22.0)	1	1
Yes	623	90	(14.4)	10.19 (3.18-32.58)	7.78 (2.39-25.38)	449	316	(70.4)	1.14 (1.10-1.18)	5.48 (3.20-9.38)	871	725	(83.2)	17.64 (12.2-25.52)	17.94 (11.78-27.34)
HIV															
Negative	-	-	-	-	-	495	286	(57.8)	1	1	972	671	(69.0)	1	1
Positive	-	-	-	-	-	57	52	(91.2)	7.6 (2.98-19.36)	391 (1.41-10.82)	87	85	(97.7)	19.06 (4.66-77.99)	9.13 (1.89-44.09)
Number of years of injecting use															
Less than 10	220	10	(4.5)	1(c)	(e)	102	43	(42.2)	1(c)	(e)	267	167	(62.5)	1(c)	(e)
10-19	224	29	(12.9)	3.12 (1.48-6.58)		179	133	(74.3)	3.97 (2.38-6.65)		325	300	(92.3)	7.19 (4.46-11.58)	
More than 19	144	48	(33.3)	10.50 (5.10-21.63)		141	124	(87.9)	10.01 (5.27-19.01)		213	204	(95.8)	13.57 (6.66-27.66)	
Frequency of injecting heroin use															
Up to twice a week	67	5	(7.5)	-	-	37	19	(51.4)	1	(e)	94	73	(77.7)	-	-
Three or more times a week	507	79	(15.6)	-	-	373	266	(71.3)	2.36 (1.19-4.66)		711	599	(84.2)	-	-

^(a)Gender was included in the multivariate analysis as control variable because it was associated to execution of HIV test.

^(b)Gender was included in the multivariate analysis as control variable because it was associated to execution of HCV test.

^(c) χ^2 for trend p-value < 0.05.

^(d)Area of SerT was included in the multivariate analysis as control variable because it was associated to execution of HBV test.

^(e)excluded from multivariate analysis: variables associated with injecting drug use (number of years of injecting use, frequency of injecting heroin use) were not included in the multivariate model because related only to the sub-group of IDUs.

The prevalence of HCV infection among the 1085 (81.5%) sample subjects was 71.2% overall and 83.2% among IDUs. For IDUs, the probability of infection increased with the number of years of injecting use. In the multivariate analysis, the factors significantly correlated with HCV infection were: older age, a low level of education, being HIV-positive and injecting use (*Table 1*).

DISCUSSION

The prevalence of HIV infection among drug users in this study is similar to the prevalence reported in the national survey of SerTs published annually by the Ministry of Health (13.8% in 2005) [3]. It is also similar to the prevalence rates reported among IDUs in Spain, Portugal and France, yet higher than the rates reported in other Western European countries.

In this study, the prevalence of HIV infection was slightly higher among women than among men possibly due to the low number of women in the sample. The gender difference in this study is also consistent with the data from the national survey of the Ministry of Health, which shows the HIV prevalence among drug users in 2005 as being 19.5% among women and 12.8% among men. Moreover, the proportion of HIV-positive women to HIV-positive men (1:3.0) is similar to that reported in Italy's National AIDS Registry (1:3.2) and in the surveillance system for new HIV diagnoses (1:2.4) [1].

In this study, it was not possible to determine how the HIV-infected non-injecting users (prevalence of 1.6%) acquired the infection. It is noted that in many countries the prevalence of HIV infection among non-injecting users has increased (with a simultaneous decrease among IDUs) and this increase has been correlated with sexual transmission [5, 6]. Furthermore, the prevalence of the HIV infection among non-injecting users in Italy is similar to the prevalence among heterosexual who do not use drugs but have sexually transmitted infections [7], confirming the role of unsafe sex in the spread of HIV among non-injectors.

As reported in other studies [8], HIV infection was also correlated with older age, which is consistent with the finding that older drug users who have engaged in drug use longer have consequently been exposed longer to risk factors for infection. Moreover, older drug users were engaging in drug use in a period in which infection was much more widespread among drug users, thus increasing their risk.

The finding that the prevalence of HIV infection was higher in Northern Italy than in Central and Southern Italy confirms the north-south gradient among both drug users and the general population [1]. This gradient can be attributed to the fact that the initial ports of entry of HIV infection in Italy were urban areas in the north and that the HIV epidemic affected South Italy later [9]. Although

geographic differences in the implementation of harm-reduction programs and prevention campaigns could theoretically account for these differences, these initiatives have been implemented uniformly nationwide. As also reported in other international studies [10], HIV infection was correlated with being unemployed, showing that socioeconomic disadvantages may contribute to increasing the probability of engaging in behaviours at risk. No significant correlation was found with level of education.

With regard to HBV infection, the 60.7% prevalence in our study is similar to that found in other studies among drug users in Italy [11], yet higher than the prevalence among drug users in all other European countries, with even greater differences if considering only IDUs [12]. The proportion of HBsAg-positive individuals was twice as high as the proportions for Greece and Portugal, which have the highest prevalence of HBsAg among IDUs in Europe [12]. However, this high prevalence was not correlated with any risk factor that could explain this marker's persistence. Italy began a national HBV vaccination program in 1991, and approximately 29% of the individuals in our study had been vaccinated. However, far from being eradicated by the vaccination campaign, HBV continues to circulate among young drug users. In our study, HBV infection was also correlated with unemployment, which is consistent with the recently reported correlation with socio-economic disadvantages [13]. Again, no correlation with level of education was found.

IDUs had a much higher probability of acquiring infection than non-injectors, confirming the role of intravenous transmission. Finally, HBV infection was correlated with HIV infection, probably because of the similar transmission modalities. For this reason, SerT personnel should not underestimate the increased risk of HBV infection among HIV-positive drug users and counselling should be provided to HIV-positive users to undergo HBV testing.

Of the three infections considered, the prevalence was highest for HCV infection (71.2%). Among the IDUs, the prevalence was even higher (83.2%); in Europe, prevalence higher than 80% among IDUs has only been observed in Estonia, Latvia, Romania, and Portugal [12]. In 2005, 36% of all cases of acute HCV infection in Italy were attributable to problem drug use [2]. The high rate of transmission of HCV among intravenous drug users [14] can explain why the majority of IDUs are infected with HCV, irrespective of other drug-using behaviour. A very high prevalence was also found among non-IDUs, compared to that reported in the general population (3.7%) [2], a finding which deserves further investigation.

Advanced age was also correlated with HCV infection, which is consistent with data provided by the Ministry of Health and SEIEVA [3, 2]. HCV infection was correlated with both unemployment

and a low level of education, confirming the role of disadvantaged socioeconomic status [11] and indicating that drug users often suffer from some degree of social exclusion, which is closely related to vulnerability and deterioration of health. Finally, as found for HBV infection, injecting use and HIV infection were correlated with HCV infection.

Although we did not include duration of injecting use in the multivariate analysis, the results of the univariate analysis showed that this was correlated with all three infections, confirming the close correlation between injecting use and the acquisition of blood borne infections. These data show the need for prevention programs, especially among drug users who have recently begun to engage in injecting use.

This study has several limitations. The results only refer to a sample of drug users attending the SerTs, who are not necessarily representative of the entire drug-using population. Moreover, the cross-sectional design did not allow us to draw conclusions in terms of causality; only general correlations could be made. Furthermore, serology results for HIV, HBV, and HCV were not available for all participants. Recall bias regarding drug use and sexual behaviour may also have affected the results, reducing the correlation of these variables. Finally, we could probably have obtained better results, had we performed separate analyses for injecting and non-injecting drug users, even though in our sample non-injectors were very under-represented.

Despite these limitations, the results confirm that injecting drug use continues to be an important risk factor for blood borne infections. We recommend that all drug users attending SerT be periodically screened for HIV, HBV, and HCV, including non-injectors, who are often assumed to be at low risk for parenteral infections. Strikingly high prevalence rates were observed among IDUs for both HCV and HBV infection, particularly among young IDUs, suggesting that these viruses are widely circulating

in this population and that targeted prevention programs are urgently needed. HBV vaccination should be actively offered to all HBV-negative drug users. Finally, in this study, sexual behaviour, compared to injecting behaviour, seems to have played a minor role in transmission; however, it has been suggested that the increasing use of non-injecting drugs may lead to an increased spread of infections through sexual contact [15, 6]. High priority should be given to harm-reduction programs for all drug users. In particular, safe-sex programs should be implemented in consideration of the increase in the non-injecting use of drugs.

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