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Risk factors for monoinfections and coinfections with HIV, hepatitis B and hepatitis C viruses in northern Spanish prisoners

J. PALLÁS[1]*, C. FARIÑAS-ÁLVAREZ[2], D. PRIETO[2] J. LLORCA[2] AND M. DELGADO-RODRÍGUEZ[2]

[1] *Provincial Prison, Santander* [2] *Department of Medicine, Division of Preventive Medicine and Public Health, University of Cantabria, Santander, Spain*

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SUMMARY

A cross-sectional study was conducted in prisons of Cantabria (northern Spain) from June 1992 to December 1994. Inmates were asked to participate in a survey on prevalence and risk factors for monoinfections and coinfections with HIV, HBV and HCV. Crude and multiple odds ratios of risk factors were calculated (by polychotomous logistic regression). Prevalence of coinfections was higher than that of monoinfections. IDU risk factors were the main independent variables associated with monoinfections and coinfections with these agents. The strength of association increased with the degree of coinfection for IDU risk factors and penal status, e.g. duration of injecting drug use for more than 5 years yielded an adjusted OR ranging from 1·3 (95% CI: 0·4–5·1) for HBV monoinfection to 180 (95% CI: 61·0–540·0) for HIV–HBV–HCV coinfection. In comparison, sexual behaviours were less important than IDU risk factors.

INTRODUCTION

Since the first AIDS cases were notified from Spanish prisons, the number of cases has increased [1], and AIDS has become the leading cause of death in prison [2]. The prison population in Spain shows a high prevalence of injecting drug users (IDU) [3, 4], the main risk factor for HIV in prison [5–7]. Injecting drug use also increases the risk of HBV and HCV infections [8–10]; so it is very likely that a patient infected with HIV also will be infected with HBV and/or HCV [11–16].

Information regarding risk factors for coinfections (HIV, HBV, HCV) is scarce, although the epidemiology of these three infections is well-known. The high prevalence of these infections (HIV, HBV, HCV) in Spanish prisons [17–20] offers a good opportunity to study the risk factors for coinfections as opposed to monoinfections. This was the major objective of this report.

* Author for correspondence: Division of Preventive Medicine & Public Health, School of Medicine, University of Cantabria, Av. Cardenal Herrera Oria s/n, 39011-Santander, Spain.

METHODS

A cross-sectional study was carried out among new entrants in the two prisons of the province of Cantabria, northern Spain, from 1 June 1992 to 31 December 1994. Inmates entering at the two participating prisons (978 inmates in the provincial jail of Santander and 865 in the El Dueso prison; total: 1843 inmates) were asked to consent to be interviewed and to submit a blood sample for HIV, HBV and HCV testing, and we ensured that confidentiality of information was maintained. Those inmates who accepted participation ($n = 1640$) were given an appointment 7 days later. Of those, the number of eligible subjects who remained in prison for at least 7 days was 1215. On the day of appointment the participants were sent to the infirmary of the peni-

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tentiary to fill in a questionnaire and to draw a blood sample for serologic testing.

A standard pretested questionnaire was administered by trained interviewers, including data about sociodemographic variables, penal status and drug use behaviour (age at first use, duration, parenteral use in the past 5 years, frequency, etc.). Also, a history of risk behaviours was collected: sharing of injection equipment, use of other sharp-cutting objects, tattoos, previous transfusions and sexual behaviour. Information on the history of these behaviours was inquired about for the past 5 years, except for the number of sexual partners that was only asked for the last year.

Blood was collected using two *vacutainer* tubes. The material was then prepared for examination and/or stored in a −70 °C freezer according to standard procedures. HIV-1 antibody testing was carried out with an enzyme immunosorbent assay [21] using second generation and Western blotting techniques [22]. The tests used to detect HBV infection were enzyme-linked immunosorbent assay (ELISA) for anti-HBc, HBeAg, and anti-HBe, and radioimmunoassay for HBsAg. A second generation ELISA was used to detect antibodies to HCV. Reactivity in the band against the proteins of the core NS4 and NS5 was used for verification of anti-HCV results.

Prevalences of monoinfection or coinfection with HIV, HBV and HCV were calculated. Odds ratios (OR) and 95% confidence intervals (CI) were used to quantify the associations between risk factors and viral infections (HIV, HBV and HCV).

ORs were adjusted for several variables by polychotomous logistic regression analysis; the polychotomous logistical model permitted the calculation of the influence of an independent variable for more than two outcomes (monoinfection by HIV, HBV and HCV, or coinfection by HIV–HBV, HIV–HCV, HBV–HCV and HIV–HBV–HCV). The inmates with negative serology to HBV, HCV and HIV were always the referent group ($n = 326$). All statistics presented came from polychotomous logistic regression models, with a different model for each covariate analysed. Some continuous variables, such as duration of IDU, number of sexual partners and time in prison were categorized in some analyses. The variables included in the model of regression were those that met the criteria for a confounder. Confounders were identified using stratified analyses, stepwise polychotomous logistic regression, and information from previous studies [23]. In the final model those variables that changed the coefficient of the independent variable more than 10% were retained [24]. No problem of colinearity was observed. Explicit statistical test for trend across exposure levels in continuous variables and in categorical factors with more than two categories were performed following the recommendations by Thompson [25]. HIV–HCV coinfection (11 cases), HIV–HBV coinfection (3 cases), and HIV monoinfection (4 cases) were excluded from the polychotomous logistic regression analyses due to the small number of cases.

To assess if a risk behaviour influenced the number of viral infections (from zero to triple infections), Poisson regression analysis was used taking as dependent variable the number of viral infections. A model was constructed for every risk factor, including the same variables as for the polychotomous logistic regression analysis. If a statistically significant coefficient was obtained it suggested that the variable was related to the number of infections. Statistical analyses were performed using the BMDP Statistical Package (7.0 release) [26], and Stata Intercooled 5.0 [27].

RESULTS

Of 1215 incarcerated subjects who met the eligibility criteria, 1015 agreed to answer the questionnaire and 693 also accepted blood drawing for serologic testing. Thus, the participation rate was 83·5% on the questionnaire and 57% for serological testing. There were no significant demographic differences in serological testing by age, sex, educational level, and history of incarceration observed between participants ($n = 693$) and non-participants ($n = 322$). Those inmates who refused everything the day of admission ($n = 203$), stayed in prison for less than 7 days ($n = 225$), or refused to participate the day of appointment ($n = 200$), were also compared using the demographic data provided by the prison chart on admission; no significant difference was observed in comparison with participants ($n = 628$; analysed variables: age, sex, and number of incarcerations; 91·7% male; mean age: 30·6 years, standard deviation: S.D. = 9·9; mean number of incarcerations: 4·5, S.D. = 4·0). Behavioural risk factors could not be compared as this information was lacking on non-participants.

Ninety-five percent of the study population were males. The mean age was 30·7 years (S.D. = 8·9). The educational level was low: 47·5% had secondary

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Table 1. *Demographic and behavioural risk factors according to degree of infections with HBV, HCV and HIV among male inmates, Northern Spain, 1992–4*

Variable	No infection $n = 326$ (47·1)	HBV monoinfection $n = 77$ (11·1)	HCV monoinfection $n = 50$ (7·2)	HBV–HCV coinfection $n = 136$ (19·6)	HIV–HBV–HCV coinfection $n = 86$ (12·4)
Sex male	311 (95·4)	71 (92·2)	47 (94·0)	132 (97·1)	81 (94·2)
Age (years)					
$\leqslant 20$	25 (7·7)	4 (5·2)	9 (18·0)	13 (9·6)	5 (5·8)
21–25	61 (18·7)	10 (13·0)	15 (30·0)	42 (30·9)	16 (18·6)
26–30	77 (23·6)	12 (15·6)	16 (32·0)	35 (25·7)	33 (38·4)
31–35	75 (23·0)	16 (20·8)	6 (12·0)	32 (23·5)	20 (23·3)
> 35	88 (27·0)	35 (45·5)	4 (8·0)	14 (10·3)	12 (14·0)
Educational level					
Primary school	108 (33·1)	37 (48·1)	19 (38·0)	51 (37·5)	45 (52·3)
Secondary school	153 (46·9)	29 (37·7)	23 (46·0)	69 (50·7)	35 (40·7)
Higher than secon.	30 (9·2)	6 (7·8)	8 (16·0)	13 (9·6)	4 (4·7)
Not available	35 (10·8)	5 (6·4)	— (0·0)	3 (2·2)	2 (2·3)
Duration of the heroin use					
Never	300 (92·0)	64 (83·1)	19 (38·0)	31 (22·8)	6 (7·0)
$\leqslant 5$ years	13 (4·0)	10 (13·0)	12 (24·0)	30 (22·1)	11 (12·8)
> 5 years	13 (4·0)	3 (3·9)	19 (38·0)	75 (55·1)	69 (80·2)
Needle-sharing	2 (0·6)	3 (3·9)	11 (22·0)	58 (42·6)	53 (61·6)
Tattoos	39 (12·0)	14 (18·2)	23 (46·0)	48 (35·3)	43 (50·0)
Blood transfusions	11 (3·4)	3 (3·9)	3 (6·0)	7 (5·1)	10 (11·6)
Sexual partners > 2	92 (28·2)	21 (27·3)	18 (36·0)	49 (36·0)	34 (39·5)
Not available	31 (9·5)	7 (9·1)	3 (6·0)	15 (11·0)	13 (15·1)
Anal sex	23 (7·1)	9 (11·7)	5 (10·0)	23 (16·9)	17 (19·8)
Homosexual practice	3 (0·9)	2 (2·6)	1 (2·0)	4 (2·9)	4 (4·7)
Not available	1 (0·3)	— (0·0)	— (0·0)	— (0·0)	— (0·0)
Reincarceration	111 (34·0)	44 (57·1)	30 (60·0)	93 (68·4)	72 (83·7)
Not available	34 (10·4)	5 (6·5)	— (0·0)	3 (2·2)	1 (1·2)
Time cumulative in prison (reincarcerates)					
$\leqslant 5$ years	98 (88·3)	34 (77·3)	23 (76·7)	81 (87·1)	57 (79·2)
> 5 years	13 (11·7)	10 (22·7)	7 (23·3)	12 (12·9)	15 (20·8)

* Values within parentheses are percentages.

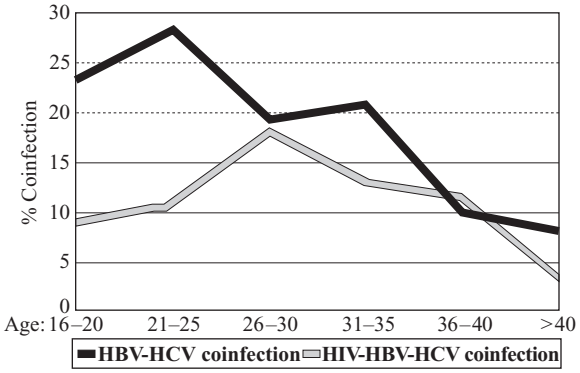

Fig. 1. Prevalence of HBV, HCV and HIV coinfections among male inmates at different age intervals, Northern Spain, 1992–4.

school and 37·2% had primary school or less. Previous incarceration was reported by 384 (55·4%) inmates, with a mean of 4·2 incarcerations (S.D. = 3·9), and a cumulative lifetime of incarceration greater than 2 years (mean: 2·3; S.D. = 3·4). The proportion of IDUs in the study population was 32·3%. Injectors had been injecting for an average of 8·6 years (S.D. = 4·5), and most IDUs shared needles (60·7%). For other parenteral risk factors, 25·7% were tattooed, 6·3% shared sharp-cutting objects and 5·3% reported a history of blood transfusion. Regarding sexual behaviour, 32·3% of inmates had more than two partners for the preceding year (mean; 3·0; S.D. = 6·9) and fewer inmates reported anal sex or homosexual contact for the last 5 years (12% and 2·5%, respectively). The S.D. for some of the continuous variables was greater than the means (duration of incarceration and number of sex partners), and this was due to the existence of two differentiated groups in these variables (bimodal distribution).

The frequency of monoinfections and coinfections, demographic characteristics and behavioural risk factors are shown in Table 1. The overall seroprevalence was 43·4% for HBV, 40·8% for HCV and 14·9% for HIV. Inmates infected with HIV presented a high degree of coinfection with HBV and HCV. The prevalence of HBV-HCV coinfection was 19·6%, whereas triple infection (HIV–HBV–HCV) was 12·4%. Other coinfections were: HIV–HCV coinfection (11 cases; 1·6%), and HIV–HBV coinfection (3 cases; 0·4%). The most prevalent monoinfection was HBV, whereas HIV monoinfection was very uncommon (4 cases; 0·6%). The highest prevalence of coinfection with HBV and HCV was found among 21–25 year old inmates (28·4%), whereas HIV–HBV–HCV infection showed the highest prevalence in the age group 26–30 years (Fig. 1). There were no differences in the frequency of behavioural risk factors according to age.

Table 2. *Association between IDU risk factors ad HBV, HCV and HIV infections in prison inmates, Northern Spain, 1992–4*

Variable/ effect	Adjusted OR (95% CI)*
IDU > 5 years†	
HBV monoinfection	1·3 (0·4–5·1)
HCV monoinfection	19·0 (7·5–46·0)
HBV–HCV coinfection	43·0 (20·0–93·0)
HIV–HBV–HCV coinfection	180·0 (61·0–540·0)
Duration of the injecting drug use (per year of use)†	
HBV monoinfection	1·2 (1·0–1·3)
HCV monoinfection	1·4 (1·3–1·6)
HBV–HCV coinfection	1·6 (1·4–1·7)
HIV–HBV–HCV coinfection	1·7 (1·6–1·9)
Needle-sharing†	
HBV monoinfection	2·7 (0·3–22·0)
HCV monoinfection	6·7 (1·3–35·0)
HBV–HCV coinfection	14·0 (3·1–67·0)
HIV–HBV–HCV coinfection	36·0 (7·1–180·0)
Tattoos†	
HBV monoinfection	1·7 (0·8–3·5)
HCV monoinfection	3·2 (1·4–7·1)
HBV–HCV coinfection	1·2 (0·6–2·5)
HIV–HBV–HCV coinfection	2·3 (1·0–5·3)
Sharing sharp-cutting objects†	
HBV monoinfection	1·4 (0·3–8·1)
HCV monoinfection	1·4 (0·2–9·1)
HBV–HCV coinfection	3·5 (0·8–15·0)
HIV–HBV–HCV coinfection	4·8 (1·0–24·0)
History of blood transfusions†	
HBV monoinfection	0·8 (0·2–3·7)
HCV monoinfection	2·0 (0·4–10·0)
HBV–HCV coinfection	2·6 (0·7–9·0)
HIV–HBV–HCV coinfection	6·9 (1·7–28·0)

* OR, odds ratio. CI, confidence interval.
† Adjusted for age, sex, educational level, prior incarceration, duration of injecting drug use and number of sexual partners.

Regarding females inmates ($n = 34$), 15 showed negative serology for all viruses, 6 showed HBV monoinfection, 5 triple infections, 4 HBV-HCV coinfection, 3 HCV monoinfection and 1 HIV–HCV coinfection. No epidemiological difference was found in education level, age, and other risky behaviours variables according to gender. Eleven females were IDUs, and five female inmates shared injection equipment.

The association between IDU risk factors and viral infections is shown in Table 2. An increasing risk

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Table 3. *Association between sexual behaviour and HBV, HCV and HIV infections in male inmates, Northern Spain, 1992–4*

Variable/ effect	Adjusted OR (95% CI)*
Number of sexual partners > 2 (Ref. ⩽ 2)†	
HBV monoinfection	1·1 (0·6–2·1)
HCV monoinfection	1·4 (0·7–2·8)
HBV–HCV coinfection	1·5 (0·9–2·4)
HIV–HBV–HCV coinfection	2·0 (1·1–3·7)
Number of sexual partners (per each additional partner)†	
HBV monoinfection	0·9 (0·9–1·0)
HCV monoinfection	1·0 (0·9–1·0)
HBV–HCV coinfection	1·0 (1·0–1·1)
HIV–HBV–HCV coinfection	1·0 (1·0–1·1)
Anal sex‡	
HBV monoinfection	2·1 (0·9–5·1)
HCV monoinfection	1·2 (0·4–3·5)
HBV–HCV coinfection	2·1 (1·0–4·3)
HIV–HBV–HCV coinfection	2·3 (1·0–5·3)
Homosexual practice§	
HBV monoinfection	2·2 (0·4–14·0)
HCV monoinfection	1·9 (0·2–20·0)
HBV–HCV coinfection	2·6 (0·5–13·0)
HIV–HBV–HCV coinfection	2·8 (0·5–16·0)

* OR, odds ratio. CI, confidence interval.
† Adjusted for age, sex, educational level, prior incarceration and anal sex.
‡ Adjusted for the same variables as †, plus number of sexual partners.
§ Adjusted for the same variable as ‡, except anal sex.

parallel to the number of infections was documented. For instance, a duration of injecting drug use for more than 5 years showed an adjusted OR ranging from 1·3 (95% CI: 0·4–5·1) for HBV monoinfection up to 180 (95% CI: 61·0–540·0) for HIV–HBV–HCV infection; this variable was significantly related to the number of viral infections in the Poisson regression analysis ($P < 0·001$). Moreover, there was an increase in the risk per year of use for all infections ($P < 0·001$), apart from HBV monoinfection. Needle-sharing was also a risk factor for coinfections, increasing the risk of triple infection in comparison to HBV–HCV coinfection and monoinfections; it was also related to the number of viral infections in the Poisson regression ($P < 0·001$). For other parenteral risk factors there were no significant risk gradients. However, there was a statistical association between having a tattoo and HCV monoinfection and triple infection. Blood transfusions and shared sharp-cutting objects were also significant predictors of triple infection.

Table 4. *Association between demographic and penal status risk factors and HBV, HCV and HIV infections in male inmates, Northern Spain, 1992–4*

Variable/ effect	Adjusted OR (95% CI)*
Time cumulative in prison > 5 years†	
HBV monoinfection	4·5 (1·6–13·0)
HCV monoinfection	15·0 (4·0–57·0)
HBV–HCV coinfection	10·0 (3·6–28·0)
HIV–HBV–HCV coinfection	31·0 (9·6–100·0)
Time cumulative in prison (risk per year)†	
HBV monoinfection	1·3 (1·2–1·5)
HCV monoinfection	1·4 (1·2–1·7)
HBV–HCV coinfection	1·3 (1·2–1·5)
HIV–HBV–HCV coinfection	1·4 (1·2–1·6)
Reincarceration†	
HBV monoinfection	2·2 (1·2–4·0)
HCV monoinfection	3·7 (1·8–7·4)
HBV–HCV coinfection	5·3 (3·2–8·8)
HIV–HBV–HCV coinfection	15·0 (6·8–33·0)

* OR, odds ratio. CI, confidence interval.
† Adjusted for age, sex, educational level and number of sexual partners.

Sexual behaviour was related to triple infection (Table 3). For example, in inmates having two or more sexual partners the adjusted OR for HIV–HBV–HCV infection was 2·0 (95% CI: 1·1–3·7). However, risk of infection did not increase with each additional sexual partner ($P > 0·05$), and the relationship with the number of viral infections in the Poisson regression was not significant ($P = 0·123$).

A previous incarceration was a significant predictor, showing a greater association (higher adjusted ORs) for HBV–HCV coinfection and HIV–HBV–HCV coinfection than for monoinfections (Table 4); this variable was significantly related to the number of viral infections in the Poisson regression ($P < 0·001$). Moreover, the time spent in prison was an important risk for all infections (P for trend $< 0·001$), showing a greater association with coinfections ($P < 0·001$).

DISCUSSION

There were several potential limitations of this study. One was the low participation rare among the eligible inmates, although this was consistent with other reports on prisoners [28, 29]. Several reasons have been offered to explain the low participation rate in these kinds of studies: low motivation and low levels of education among many inmates, fear of knowing

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the result of serologic testing [30, 31], or distrust of the confidentiality of data under a judicial process [32]. Also, although there were no demographic differences between participants and non-participants, we could not adequately assess whether selection bias was present in our study as information on risk factors in non-participants was lacking.

Another factor that may limit the validity of the conclusions of this study was sample size; several groups of monoinfections and coinfections (i.e. HIV monoinfection or HIV–HBV coinfection), had to be excluded from the analysis because of small sample size. Other groups included were still sparse, and it may have produced a lack of statistical power to detect some associations.

The overall prevalence of HIV infection was 14·9%, lower than those reported in other Spanish prisons [17, 33], although this figure was higher than those found in other western countries [8, 31, 34–38]. The frequency of HBV and HCV was within the range found in western countries [8, 17, 39, 40].

Most individuals were infected with more than one virus, and these results differed from those found in studies done in general populations, which have reported lower proportions of coinfection [41–43]. The strong association between HBV and HCV [44] and the high degree of coinfection with HIV in prisoners have been observed previously in other studies carried out in IDUs [45, 46]. However, previous reports have not analysed whether there are epidemiological differences between monoinfections and coinfections by polychotomous logistic regression.

The finding that the prevalence of HIV–HBV–HCV infection peaked at older ages than HBV–HCV coinfection suggests that the last acquired infection was HIV. This might be explained by lower resistance of HIV to environmental conditions in comparison to hepatitis viruses [47], and to different transmission dynamics of these viruses [48], therefore needing more intensive exposures to achieve successful transmission. Nevertheless, this could be also due to the higher prevalence and existence of risk groups (IDU, tattooing, etc.) in older inmates. In our study the mean age of HIV positive inmates was 29·0 years (S.D. = 6·4), a younger age than that shown by Davies and colleagues [49].

As expected the risk factors for coinfections found in our study were similar to those found for monoinfections, but with a greater strength of association, mainly among IDU risk factors. These results suggest that the presence of a risk factor facilitates the transmission of several viruses. However, the small number of monoinfections and some coinfections forces us to be cautious and is a limitation for explaining the observed gradient of association between risk factors and HBV, HCV and HIV infections.

The association between injecting drug use and viral infections in this population was strong and included an increasing gradient in the degree of association with the number of viruses, suggesting that it may be the major route of transmission among inmates admitted to Spanish prisons. The frequency of IDU is similar or lower than that reported by other studies in prisons [18, 33, 36, 50]. Most IDUs shared injection equipment, and our figure was intermediate according to other studies among inmates [28, 36, 51]. Duration of injecting drug use and sharing-needles were the main risk factors for viral coinfection. In addition, it has been documented that short-term IDUs show a high risk of HIV, HBV and HCV infections [52]. Therefore, these findings support the hypothesis that the risk of coinfection increases with length of exposure to risky behaviours.

In our study, risky sexual practices did not lead to an increase in the strength of association with the number of virus infections. The results regarding the number of sexual partners were similar to those reported by Dufour and colleagues for HIV prevalence [36]. On the other hand, the high proportion of inmates with three or more sexual partners during the last year (32·3%) and practising anal sex (12%) suggested a high level of risky sexual behaviour in people entering our prisons. These results suggest that in our population sexual behaviour loses importance in relation to parenteral risk factors, thus confirming previous observations [46]. Homosexual behaviour was not a significant risk factor in our study, probably due to its low prevalence (2·5%), and this agrees with other studies [53, 54]. The actual prevalence of homosexuality may be higher, but the stigma of this behaviour within prison could cause underreporting.

An interesting finding was that the penitentiary itself could be an independent risk factor for monoinfection and coinfection. Reincarceration as well as time spent in prison were shown to be independent risk factors for the three infections. Also, all the variables related to penal status increased the number of viral infections. Previous reports have shown an association between imprisonment and HIV, HBV and HCV infection [49, 55, 56]. However, caution is

needed regarding this finding. This was a cross-sectional study, so we could not determine whether infections were acquired before or after incarceration. The main risk factors were controlled for by multivariate analyses, but other unknown variables could be responsible for the increase in risk found with reincarceration. This could be due to a greater risk of sharing-needles among drug using inmates on admission to jail [36, 54, 57, 58]. This could explain why the risk of viral infections increases with a previous incarceration and with a longer time in prison associated with reincarceration (64% of reincarcerates remained at least 1 year in prison). Another explanation could be that prison is a place where several risk factors act together.

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