

Hepatitis C virus infection and prisoners: Epidemiology, outcome and treatment

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Abstract

The studies on hepatitis C virus (HCV) infection in prison populations are few and mostly cross-sectional. We analyzed prevalently the articles appearing on PubMed in the last ten years. HCV infection is frequent in prisoners, prevalences ranging from 3.1% to 38% according to the HCV endemicity in the geographical location of the prison and in the countries of origin of the foreign prisoners and to the prevalence of intravenous drug use, which is the most important risk factor for HCV infection, followed by an older age of prisoners and previous prison terms. HCV replication in anti-HCV-positive cases varies from 45% to 90% in different studies, and the most common HCV genotypes are generally 1 and 3. The response to antiviral treatment is similar in prisoners to that of the general population. Unfortunately, treatment is administered less frequently to prisoners because of the difficulties in management and follow-up. The new directly acting antivirals offer a good therapy option for inmates because of their good efficacy, short duration of treatment and low incidence of side effects. The efforts of the prison authorities and medical staff should be focused on reducing the spread of HCV infection in prisons by extending the possibility of follow-up and treatment to more prisoners with chronic hepatitis C.

Key words: Prisoners; Management; Treatment; Care; Chronic hepatitis C

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Core tip: Hepatitis C virus (HCV) infection in prisoners is

a social health problem: It is more frequent than in the general population, but access to proper management and treatment is more difficult. In this setting HCV infection can be easily transmitted due to overcrowded conditions, sharing supplies and particularly by drug use. In the past, HCV treatment was rarely administered to prisoners, often because they did not stay in the same structure long enough. Also, the risk of HCV re-infection is high in inmates. New policies should be applied to guarantee prisoners the same care as the general population, particularly in view of the new, shorter and more effective anti-HCV treatments.

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INTRODUCTION

The United Nations Basic Principles for the Treatment of Prisoners state that prisoners "shall have access to the health services available in the country without discrimination on the grounds of their legal situation"^[1]. Unfortunately, this basic principle has been infrequently applied in real life and in most countries prisoners have a lesser possibility of assistance and care than other citizens^[2].

Hepatitis C virus (HCV) infection is more frequently detected in inmates than in the general population^[3,4], the highest prevalence being reported in Central Asia (38%) and Australasia (35%)^[3]. These high prevalences are due mostly to unsafe lifestyles and family, psychiatric and social problems, conditions often experienced by prisoners before incarceration. Intravenous drug use (IVDU), tattooing and promiscuous sexual contact^[5] are the main risk factors for acquiring HCV infection. Once in prison, overcrowding, violence, separation from family and emotional problems are additional reasons^[6] that may induce inmates to start or continue unsafe habits. An estimate of the incidence of new HCV infections in prisons exceeds 30 per 100 persons per year^[7,8].

Proper treatment of chronic hepatitis C in prison is rare for social and educational reasons^[9,10] and, not least, because most inmates with HCV infection remain unaware of their virological condition. Several other barriers may prevent HCV inmates from being admitted for treatment: Individual problems (drug abuse, stress, fear, lack of confidence) and social problems (stigma, discrimination, difficulty to relate to the health personnel)^[11]. Another obstacle may be the lack in a prison of a liver disease specialist, a problem that can be overcome with the use of telemedicine^[12].

Although many prisoners are incarcerated for long periods, the average length of stay in the same prison can be weeks or months in several cases^[13,14], which

makes it difficult to complete the clinical itinerary from screening to post-treatment follow-up.

The prison authorities and physicians should implement strategies to improve the diagnostic and therapeutic approach to HCV in prisoners, general screening for the anti-HCV antibody being the first step in this approach. Prisoners with chronic HCV infection should undergo a full diagnostic procedure and clinical staging before being considered for treatment, since inmates with HCV-related chronic hepatitis can achieve a sustained virological response with the same frequency as free patients^[15].

Because of the numerous obstacles mentioned above, only a few studies on HCV infection in prisons have been carried out to date, and directives issued by experts^[16] are often not properly followed. Because of complexity of the subject and in order to analyze more recent aspects of the problem, we evaluated prevalently the articles appearing on Pubmed in the last ten years. We used a combination of the following keywords: "prison", "prisoners", "inmate", "HCV infection", "intravenous drug use", "epidemiology", "chronic hepatitis", "cirrhosis", "treatment", "interferon", "ribavirin", "directly acting antivirals (DAA)", "sofosbuvir", "telaprevir", "boceprevir", to find articles focusing on the epidemiology, clinical outcome and treatment of HCV infection in prisons.

EPIDEMIOLOGY OF HCV INFECTION IN PRISONS

Table 1 shows the results of the majority of the studies performed worldwide on the anti-HCV prevalence in prisoners^[17-42]. These rates ranged over the years from 3.1% to 38%, in relation to the endemicity of HCV infection in the geographical location of the prison and in the countries of origin of foreign prisoners as well as the prevalence of IVDU in the different studies. The lowest anti-HCV prevalence (3.1%) was reported by Santos *et al*^[18] in 422 inmates held in two prisons, one for males and one for females in the State of Sergipe in Brazil, where only 10% of the detainees stated IVDU. In contrast, the highest prevalence of HCV infection was reported by Reekie *et al*^[28] in prisoners in Australia investigated in 2004. The same Author found lower rates in subsequent studies evaluating HCV infection in the inmates of all Australian prisons, 33.3% in 2007 and 23.1% in 2010, regardless of IVDU.

Taylor *et al*^[23], in a national cross-sectional study conducted in Scotland, showed an overall prevalence of HCV infection of 19% in a population of 4904 inmates, 53% in prisoners with a history of IVDU and 3% in those without. Another national cross-sectional study evaluated 1876 inmates randomly selected among imprisoned individuals aged over 18 in France and in French overseas departments^[26] and reported an anti-HCV prevalence of 4.8%. Alvarez *et al*^[29] documented a 10.1% prevalence of anti-HCV- positive cases among 2788 inmates held in two prisons in New York State,

Table 1 Hepatitis C virus prevalence in different studies on prisoners

Ref.	Year of screening	Country	Type of study	Number screened/total	Type of screening	HCV prevalence
Adjei <i>et al</i> ^[31]	2004/5	Ghana	C-S 8 prisons; inmates vs staff	1336/7652 vs 445/2139	C + Q	18.7% vs 18.7%
Almasio <i>et al</i> ^[16]		Italy				38%
Alvarez <i>et al</i> ^[29]	2009/13	United States	C-S	2788	C + Q + Clinical records	10.1%
Babudieri <i>et al</i> ^[42]		Italy	C-S 8 prisons	973		38%
Barros <i>et al</i> ^[20]	2007/8	Brazil	C-S	148/150	C + I	6.1%
Brandolini <i>et al</i> ^[17]	2006	Italy	C-S	695/965	HCV History + C	22.4%
Hennessey <i>et al</i> ^[36]	1999/2000	United States	C-S	1292 HIV-positive	Stored blood + medical records	13%
Kazi <i>et al</i> ^[33]	2007/8	Pakistan	C-S	357	C + Q	15.2%
Kheirandish <i>et al</i> ^[37]	2006	Iran	C-S	454/499	C + I	80%
Luciani <i>et al</i> ^[24]	2005/9	Australia	Prospective cohort study	210 HCV Ab -	C + Q + payment+ follow-up	Incidence 14.8 per 100/yr
Macalino <i>et al</i> ^[32]	1998/2000	United States		4269/5390 446 incidence study		23.1% 0.4 per 100/yr
Mahfoud <i>et al</i> ^[30]	2007/8	Lebanon	C-S	580/35500	Random+ C + Q	3.43%
Marco <i>et al</i> ^[41]		Spain	Observational and C-S 18 prisons	371	Q	22.7%
Meyer <i>et al</i> ^[34]	2002	Germany	C-S	1125/1176	C + I post screening	8.6%
Mohamed <i>et al</i> ^[19]		Egypt	C-S	500/1200	Random sampling + C + Q	15.8%
Nokhodian <i>et al</i> ^[40]		Iran	C-S	160	C + I	4.4%
Prasetyo <i>et al</i> ^[21]	2009	Indonesia	C-S 4 prisons	375/375	C + Q	34.1%
Reekie <i>et al</i> ^[28]	2004	Australia	C-S	588	C + Q	33.3%
	2007		C-S	536	C + Q	31.6%
	2010		C-S	618	C + Q	23.2%
Rosa <i>et al</i> ^[27]	2010/11	Brazil	Descriptive study	195/386	Random + C + Q	9.7%
Sagnelli <i>et al</i> ^[38]		Italy	C-S 9 prisons	2241/3468	Peer-to-peer education + C	22.8%
Saiz de la Hoya <i>et al</i> ^[25]	2008	Spain	C-S 18 prisons	378		22.7%
Santos <i>et al</i> ^[18]	2009/10	Brazil	C-S 2 prisons	422/519	C + Q	3.1%
Semaille <i>et al</i> ^[26]	2010	France	C-S 27 prisons	1876	Q + medical records	4.8%
Solomon <i>et al</i> ^[35]	2002	United States	C-S	3914	Educational information, C + or counseling	29.7%
Taylor <i>et al</i> ^[23]	2010/11	Scotland	C-S 14 prisons	4904/6565	C + Q	19%
Tresó <i>et al</i> ^[22]	2007/9	Hungary	C-S 20 prisons inmates vs staff	4894/14331	C + Q	Incidence > 1% 4.9% vs 0.5%

C-S: Cross-sectional; C: Consent; Q: Questionnaire; I: Interview; HCV: Hepatitis C virus.

while Macalino *et al*^[32] found a prevalence of 32.1% in a cross-sectional study involving 4260 prisoners incarcerated in Rhode Island correctional facilities. In this study the authors investigated only the inmates detained in the same prison for more than 12 mo and registered an incidence rate of 0.4 per 100 persons per year.

Cross-sectional studies in different Italian prisons published 5 years apart showed anti-HCV positivity of 38%^[42] and 22.8%^[38] in the inmates investigated.

Most of the studies listed in Table 1 were cross-sectional, performed with different aims, enrolment criteria and statistical analysis. In most studies the information on the prisoners was obtained using a pre-coded questionnaire, less frequently by oral interview^[20,34,37,40] and in only one case by doctor-to-patient interview^[35]. Some questionnaires gave no information on important socioeconomic factors, which are indicators of the level of awareness of HCV infection^[30]. In addition, it cannot be excluded that some inmates may have lied regarding certain questions, in particular those concerning IVDU and sexual behavior, probably because these behaviors are illegal or considered immoral from a social perspective. To have more reliable information

from the prisoners, educational programs or peer-to-peer communication^[38] could be organized to improve the trust relationship between the patients and medical personnel. In some studies the information was obtained from medical records, with a consequent lack of some important data^[26,27,36].

Different results were reported in two interesting studies comparing the prevalences of anti-HCV-positive cases between prisoners and members of the staff. Tresó *et al*^[22] performed a multicenter cross-sectional study in Hungary and found a significant difference in the anti-HCV rate between the prisoners (4.9%) and the wardens (0.47%), whereas Adjei *et al*^[31] found the same anti-HCV prevalence (18.7%) in prison officers and prisoners in nine prisons in Ghana, possibly reflecting an occupation-related transmission or simply the high prevalence of HCV infection in this country.

RISK FACTORS FOR THE ACQUISITION OF HCV INFECTION IN PRISONERS

The epidemiological impact of various risk factors for acquiring HCV infection has been investigated in

Table 2 Risk factors associated with hepatitis C virus, hepatitis C virus genotype and human immunodeficiency virus and/or hepatitis B virus co-infection

Ref.	HCV prevalence	Risk factors (odds ratio)	HCV genotypes (No. of patients)	Co-infection
Adjei <i>et al</i> ^[31]	18.7% vs 18.7%			
Alvarez <i>et al</i> ^[29]	10.1%	IVDU (64.8) ¹ ; sex with IVDU (8.0) ¹ ; HIV (4.3) ¹ ; STD (3.2) ¹ ; tattoo (2.9) ³ ; non-Hispanic black (2.3) ¹		
Babudieri <i>et al</i> ^[42]	38%	IVDU (10.5); tattoo (2.9)		
Barros <i>et al</i> ^[20]	6.1%	IVDU (5.9) ¹ ; > 6 in prison(4.2) ¹ ; sex with IVDU(1.4) ¹ ; age > 40 (4.4) ¹	1a (3) 1b (1) 3a (1)	
Brandolini <i>et al</i> ^[17]	22.4%	HIV +; origin; age 35-52		HIV/HCV 11.6% (60)
Hennessey <i>et al</i> ^[36]	13%	HBV (4.44) ¹ ; HIV (2.51) ¹ ; previous imprisonment (2.90) ¹		
Kazi <i>et al</i> ^[33]	15.2%	IVDU (24.32) ¹ ; surgery (2.41) ¹		
Kheirandish <i>et al</i> ^[37]	80%	History of incarceration (4.35) ¹ ; tattoo (2.33) ¹ ; first injection ≤ 25 years old (2.72) ¹		
Luciani <i>et al</i> ^[24]	Incidence 14.8 per 100/yr	IVDU-related behaviors; origin (2.63) ²		
Macalino <i>et al</i> ^[32]	23.1% 0.4%/yr	IVDU (32.44) ¹ ; increasing age > 30		
Mahfoud <i>et al</i> ^[30]	3.43%	IVDU; previous imprisonment; tattoo	1 (5) 3 (1)	
Marco <i>et al</i> ^[41]	22.7%			HIV/HCV 39
Meyer <i>et al</i> ^[34]	8.6%	IVDU; tattoo	1 (34) 2 (5); 3 (24) 4 (3)	HCV/HIV 5 HCV/BcAb 33 B/C 1.2%
Mohamed <i>et al</i> ^[19]	15.8%	IVDU (4.1) ¹ ; > 10 in prison (3.4) ¹ ; shared toiletries (3.9) ¹ ; tattoo (2.8) ¹ ; dental procedure (4.7) ¹ ; age > 45 (1.5) ¹ ; DM (3.9) ¹		
Nokhodian <i>et al</i> ^[40]	4.4%	IVDU (134.44)		
Prasetyo <i>et al</i> ^[21]	34.1%	IVDU (2.5); tattoo (3.2); piercing (3.6)	1a (14) 1c (5) 1b (1) 3a (4) 3k (4) 4a (2)	B/C 4
Reekie <i>et al</i> ^[28]	33.3% ('04) 31.6% ('07) 23.2% ('10)	IVDU; women (1.33) ³ Age ≥ 25 (1.56) ³ Previous imprisonment (2.15) ³		HIV/HCV 1 HBV/HCV 6 HBV/HCV 5 HBV/HCV 2
Rosa <i>et al</i> ^[27]	9.7%	IVDU (8.75); tattoo (3.35)		
Saiz de la Hoya <i>et al</i> ^[25]	22.7%	IVDU (24.5) ¹ ; HIV (8.4) ¹ ; Spanish (7.5) ¹ Prison > 5 yr (5.2) ¹	1a (23) 1b (12) 3 (12) 4 (16)	HIV/HCV 8.5% HBV/HCV 0.3% HBV/HCV/ HIV 1.5%
Santos <i>et al</i> ^[18]	3.1%	IVDU (23.3) ¹ ; household contact (14.1) ¹ ; syphilis (9.8) ¹ ; age > 30 (5.5) ¹	1a (6) 1b (1) 1 (3) 3 (1)	
Semaille <i>et al</i> ^[26]	4.8%	IVDU; women; > age; origin		HIV/HCV 0.08%
Solomon <i>et al</i> ^[35]	29.7%	Increasing age, max > 45 (13.51) ¹ ; women (1.32) ¹ ; HIV (4.09) ¹ ; HBV (2.69) ¹		
Tresó <i>et al</i> ^[22]	4.9%	IVDU		

¹Adjusted odds ratio; ²Hazard ratio; ³IRR. IVDU: Intravenous drug use; HCV: Hepatitis C virus; HBV: Hepatitis B virus; HIV: Human immunodeficiency virus; STD: Sexually transmitted diseases; DM: Diabetes mellitus; IRR: Incidence rate ratio.

several studies on prison populations and the results are summarized in Table 2. The main risk factor associated with HCV infection in the prison populations is IVDU. Although this risky behavior is strictly forbidden in prisons worldwide, nearly half of illicit drug users continue to use these drugs after their imprisonment. In addition, the difficulty to get sterile injecting equipment in prison results in widespread sharing of infected equipment and an increased risk of HCV transmission. A prospective Australian study conducted between 2005 and 2009^[24] on 210 anti-HCV-negative subjects with a life-time history of injection drug use observed every 6/12 mo for up to 4 years showed an incidence of HCV infection of 14.8 per 100 persons per year and that imprisonment was associated with high rates of HCV transmission.

In a cross-sectional study including four prisons in Indonesia^[21], the general prevalence of inmates with HCV infection was 34.1% (92 in IVDU and 36 in non-IVDU). A cross-sectional study^[27] in a rehabilitation center for IVDU in Iran showed that the anti-HCV prevalence reached 80%. Other forms of blood-to-blood contact such as tattooing, sharing toiletries and dental procedures were involved to a lesser extent in the transmission of HCV among prisoners.

Meyer *et al*^[34] found an anti-HCV and/or HCV-RNA prevalence of 8.6% in 1125 young prisoners, but 94% of the anti-HCV-positive were intravenous drug users.

In some studies, HCV infection was observed more frequently in female inmates than in males, reflecting the higher rates of females incarcerated for drug-related offences. Solomon *et al*^[35] investigated for the anti-HCV

prevalence the inmates entering the Maryland Division of Corrections, which includes one male and one female prison. Overall, 29.7% of 3914 prisoners were infected with HCV and the prevalence was higher in women than in men (37.9% vs 28.3%). Semaille *et al.*^[26] also described a significantly higher anti-HCV prevalence in women than in men (11.8% vs 4.5%) in French prisons.

Other risk factors related to HCV infection in prison were an older age and previous imprisonments, factors probably related to an increased exposure over time to the main risk factors. Solomon *et al.*^[35] found that the HCV prevalence progressively increased with the increase in age, from 7.9% in the age group younger than 25% to 58.5% in that over 45 years. Macalino *et al.*^[32] and Santos *et al.*^[18] found a significant association between the presence of HCV infection and an age over 30, and Mohamed *et al.*^[19] found that an age over 45 and a previous prison term were factors associated with anti-HCV positivity in inmates. A previous imprisonment was registered in the life history of the majority (89%) of anti-HCV-positive inmates in the main prison facility in Lebanon^[30].

Prisoners with HIV and/or HBV infection were more likely to be infected with HCV, probably because of the similarity in the routes of transmission of these blood-borne infections. In an Italian prison, the anti-HCV prevalence reached 89.6% in the HCV-human immunodeficiency virus (HIV) co-infected inmates and 15.5% in those without HIV infection^[17]. Similar data come from another study showing a higher prevalence of anti-HCV positivity in anti-HIV-positive patients than in the anti-HIV-negative (65.5% vs 27.5%), and in those with a present or past HBV infection (47.1%) than in those without any HBV contact (20.2%)^[35].

Virological status and clinical outcome

HCV replication in anti-HCV positive cases, as detected by the presence of HCV RNA in serum, has been reported with a rate ranging from 45% to 90% in different studies^[17,19-22,25,34].

The HCV genotype distribution varied according to the distribution in the geographical areas of the prisons and to that of the country of origin of the foreign prisoners. Meyer *et al.*^[34] performed HCV genotyping in 68 young prisoners and found genotype 1 in 50% of cases and genotype 3 in 35%; in this study genotype 1 prevailed in German inmates and genotype 3 in the prisoners from the independent states formerly part of the Soviet Union. HCV-genotype 1 predominated in Indonesian (66%)^[21] and Spanish (55%) prisons^[25]. Tyczyno *et al.*^[39] compared the HCV genotyping performed on prisoners in Poland with that of hospital patients in the same country and found that HCV genotype 3 prevailed in the prisoners (60.1%) and genotype 1 in the free patients (79.6%), most probably because genotype 3 is frequent in IVDU.

The severity of the disease associated with HCV infection and the disease progression have been

evaluated only in a few studies. Prisoners frequently showed a mild disease^[25,34] and liver cirrhosis and progression to cirrhosis were detected with a low frequency^[19]. However, most of the patients in the published studies were young and the disease progression was mostly evaluated with surrogate tests (APRI, fibroscan) and infrequently with liver biopsy^[25,34]. The mortality risks were estimated to be higher in HCV-infected than in non-infected subjects in the general population^[43], a difference that was more evident in prisoners^[44].

Treatment

Few studies have been performed to date on the treatment of chronic hepatitis C in prisoners and a sustained viral response (SVR) with standard or pegylated interferon (Peg-IFN) plus ribavirin treatments ranged from 28% to 69%^[12,43,45-52]. Encouraging results were observed in an old series in Canadian penitentiaries using standard interferon plus ribavirin, with an overall SVR of 55.9% (31.6% for genotype 1, 100% for genotype 2 and 71.4% for genotype 3)^[47]. Maru *et al.*^[52] showed an overall SVR to Peg-IFN plus ribavirin of 47.1% (43.1% for HCV-genotype 1 and 58.8% for HCV-genotypes 2 and 3), HCV-genotype 1 and liver cirrhosis being identified as predictive factors of a non-response.

Chew *et al.*^[53] obtained an overall SVR of 28% (18% for genotype 1, 60% for genotype 2 and 50% for genotype 3) with Peg-IFN plus ribavirin.

The use of second generation DAAs to treat HCV chronic infection has substantially reduced the period of treatment and of post-treatment follow-up, thus greatly improving the chances of completing treatment in prisons. A recent study comparing the cost-benefit of treatment with peg-IFN, ribavirin and boceprevir or sofosbuvir found treatment including sofosbuvir cost-effective^[54]. However, the rate of HCV re-infection after successful treatment in inmates is high, particularly in IVDU^[54,55], a priority situation warranting serious consideration. The high costs of the new DAA treatments are an important issue to be evaluated in order to extend these therapies to prison inmates^[56].

Conclusive statements

In most countries, the National Justice and Healthcare Authorities should strive to remove the enormous institutional, bureaucratic and economic barriers hampering an appropriate approach to the management of HCV infection in prisons. These institutions have a great responsibility and a fundamental role in organizing the life of prisoners, particularly of those with chronic diseases who need new costly treatments. More resources should be allocated in each country to reduce the prevalence and incidence of HCV infection in prisons and to treat all inmates already infected. The basic principle underlying this difficult issue is that prisoners in every country deserve the same healthcare treatment as the general population and to deny them this is unjust and immoral. This principle of equivalence is fundamental and is supported by the international

guidelines on prison health and prisoners' rights and the national policies in many countries^[57].

Practical advice

Reduce the spread of HCV infection in prisons by: (1) performing screening for anti-HCV as it is cost-effective, which is particularly valid for prisoners with risk factors for HCV infection^[58]; The Centers for Disease Control and Prevention recommends screening prisoners born between 1945 and 1965, the age group with the highest prevalence of HCV^[59]; (2) defining the prevalence and incidence in prisons of HCV infection; (3) performing educational programs for prisoners and prison personnel on the routes of HCV transmission, prevention measures and management of infected subjects. A successful approach based on peer-to-peer communication^[38,60,61] may improve the compliance of inmates and favor their access to screening, clinical evaluation and treatment; (4) performing regular educational programs for prisoners and staff against the discrimination of HCV-infected inmates^[62]; (5) improving the conditions of hygiene; (6) supplying the inmates with personal toiletries; (7) heightening vigilance to prevent tattooing and IVUD; and (8) providing opiate replacement therapy for drug users^[23].

Improve the access to follow-up and treatment of prisoners with chronic hepatitis C by: (1) defining the clinical condition of all anti-HCV-positive prisoners; (2) avoiding frequent transfers of inmates under treatment from one prison to another to allow the completion of therapy and post-treatment follow-up or permitting continuation treatment in another facility or outside if no longer detained^[56]; this is now easier with the introduction of the second generation DAAs, which reduce the duration of treatment and follow-up period; and (3) organizing telematic assistance to benefit from specialist's support in the management of treated patients^[56].

Sensitivity, goodwill and a willingness to cooperate by the Healthcare authorities, prison authorities and personnel are necessary.

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