



ORIGINAL ARTICLE

Prevalence of hepatitis C virus infection in patients with chronic mental disorders: The relevance of dual disorders



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Abstract

Objective: The prevalence of hepatitis C virus (HCV) infection is higher in people with psychiatric disorders compared to the general population. In addition, patients with severe mental illness are frequently affected by substance abuse, which increases the risk of blood-borne viral infections. Epidemiological studies in samples of hospitalised individuals with chronic mental disorders and dual diagnosis (DD) are lacking. The objective of this study was to investigate the prevalence of HCV infection in a sample of in-patients with severe mental illness.

Patients and methods: This was a retrospective observational study. All patients meeting selection criteria admitted to the Medium-Term Psychiatric Unit of the University of Salamanca Health Care Complex between 2007 and 2018 were included. The primary endpoint was the prevalence of HCV infection. The secondary endpoint comprised the characteristics influencing the occurrence of HCV infection in these patients.

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PALABRAS CLAVE

Hepatitis C;
Trastornos mentales;
Diagnóstico dual;
Patología dual;
Esquizofrenia

Results: A total of 497 admissions were included and patients' last admission data were considered for analyses ($n=345$). The overall prevalence of HCV infection was 3.8% and reached 14.3% among DD patients, who showed a higher prevalence than those without this condition (14.3% versus 3.1%, $p=0.009$). HCV RNA was detected in 6 individuals at diagnosis who received DAA treatment reaching sustained virological response.

Conclusions: The prevalence of HCV infection in our sample was higher than in the general population, especially among DD patients. Despite the multiple barriers to access healthcare by patients with chronic mental illness, efforts to include this population in screening and treatment are mandatory.

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Prevalencia de la infección por el virus de la hepatitis C en pacientes con trastornos mentales crónicos: la relevancia de la patología dual

Resumen

Objetivo: La prevalencia de la infección por el virus de la hepatitis C (VHC) es mayor en las personas con trastornos psiquiátricos que en la población general. Además, los pacientes con enfermedades mentales graves padecen con frecuencia abuso de sustancias, que aumenta el riesgo de infecciones virales transmitidas por la sangre. El objetivo de este estudio fue investigar la prevalencia de la infección por el VHC en una muestra de pacientes hospitalizados con trastornos psiquiátricos graves.

Pacientes y métodos: Se trata de un estudio observacional retrospectivo. Se incluyeron todos los pacientes que cumplían los criterios de selección ingresados en la Unidad de Convalecencia del Servicio de Psiquiatría del Complejo Asistencial Universitario de Salamanca entre 2007 y 2018. El criterio de evaluación principal fue la prevalencia de la infección por VHC. El criterio de evaluación secundario abarcó las características que contribuyen a dicha infección en estos pacientes.

Resultados: Se consideraron los datos del último ingreso de los pacientes incluidos ($n=345$). La prevalencia global de la infección por VHC fue del 3,8% y alcanzó el 14,3% entre los pacientes con patología dual, que mostraron una prevalencia mayor que aquellos sin esta condición (14,3 versus 3,1%, $p=0,009$). Se detectó ARN de VHC en 6 individuos en el momento del diagnóstico, que recibieron tratamiento DAA y alcanzaron una respuesta virológica sostenida.

Conclusiones: La prevalencia de infección por VHC en nuestra muestra fue mayor que en la población general, especialmente entre los pacientes con patología dual. A pesar de las barreras que dificultan el acceso a la atención sanitaria de los pacientes con enfermedades mentales crónicas, es imprescindible incluirlos en el cribado y el tratamiento.

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Introduction

Chronic hepatitis C virus (HCV) infection is a treatable condition and remains one of the most common causes of cirrhosis and hepatocellular carcinoma.^{1–4} The global seroprevalence of HCV among adults is estimated at 1% for all ages,^{5,6} similar to the data recently registered for the general population in Spain.^{7,8}

The prevalence of HCV infection is higher in people with psychiatric disorders compared to the general population, reaching nearly 20%, among psychiatric in-patients and out-patients.^{9–11} Moreover, a recent systematic review and meta-analysis showed the prevalence of blood-borne viral infections in people with serious mental illness was consistently greater than in the general population in regions with a low prevalence of blood-borne viruses, such as Europe and

North America, and equivalent to the general population in regions with a high overall prevalence, such as Asia. Regarding HCV infection, the estimated prevalence in patients with severe psychiatric disorders was 17.4% (95% CI 13.2–22.6) in North America, 4.9% (95% CI 3.0–7.9) in Europe and 4.4% (95% CI 2.8–6.9) in Asia.¹²

Substance-related disorders and addictive disorders are an important risk factor for a variety of medical and psychiatric conditions, and their co-occurrence with another mental disorder defines dual disorders (DD).¹³ Between 30% and 50% of patients diagnosed with serious mental illnesses suffer from substance abuse disorders which can lead to risk behaviours that foster viral transmission, thus increasing risk of HCV infection.^{12,14} Drug users, especially individuals with a history of injecting drugs, have the highest prevalence of HCV infection with rates as high as 14–84% in Europe.^{15,16}

These groups have unequal access to healthcare compared to the general population, which implies an increased risk of mortality and a major public health challenge.¹⁶ The availability of treatments with improved efficacy and tolerability, and the goal of eliminating HCV infection by 2030 established by the World Health Organization (WHO), should promote efforts to prevent, screen and treat HCV infection in these patients.^{15–17} Despite the high prevalence of HCV infection in people with psychiatric and/or substance abuse disorders, epidemiological studies in samples of hospitalised patients with chronic mental disorders and DD are lacking.

In light of the above, this study aimed to assess the prevalence of HCV infection and the characteristics that influenced its occurrence in patients with severe mental disorders admitted to the Medium-Term Psychiatric Unit of the University of Salamanca Health Care Complex.

Patients and methods

Study design

This observational retrospective cohort study was conducted at the Medium-Term In-Patient Psychiatric Unit of the University Hospital of Salamanca (Salamanca, Spain) in accordance with the World Medical Association Declaration of Helsinki, all its amendments, and national regulations. The study was approved by the Ethics Committee for Research with Medicines of the Salamanca Health Area (Salamanca, Spain), and patients were waived from signing the informed consent.

Participants

This study included all patients meeting selection criteria who underwent hospitalisation in the Medium-Term Psychiatric Unit of the University of Salamanca Health Care Complex between 2007 and 2018. This unit is a medium-stay facility for patients with severe and prolonged mental illness. Eligible patients were those attending any of the psychiatry units of the University of Salamanca Health Care Complex who met diagnosis criteria of a severe mental disorder and required admission to the aforementioned medium-term unit in the study period. All patients underwent HCV diagnostic tests upon hospital admission and patients with past or current intravenous drug use were not eligible.

Data collection

The study entailed retrospective collection of data from patients' medical records to assess the prevalence of HCV infection in the Medium-Term In-Patient Psychiatric Unit of the University of Salamanca Health Care Complex. Once the patients' eligibility was confirmed, socio-demographic (i.e., age, sex, marital status, environment, educational level and legal incapacity status) and clinical data (i.e., number and type of admissions, duration of hospital stay, type of discharge, mental disorder diagnosis, history of drug consumption, and serological protocol results [i.e., antibodies to hepatitis A virus (HAV), hepatitis

virus B (HBsAg), HCV (anti-HCV), human immunodeficiency virus (HIV) and *Treponema Pallidum*]) were collected. Additionally, we obtained analytical data (i.e., alanine aminotransferase [ALT], aspartate aminotransferase [AST], γ -glutamyl transferase [GGT] and platelet count) of patients who tested positive for serum anti-HCV upon admission to the Medium-Term In-Patient Psychiatric Unit. Viraemia [HCV-RNA], Child-Pugh classification, hepatic ultrasound, transient elastography, previous treatments, treatment contraindications, treatment and achievement of sustained virologic response [SVR] data of treated patients were also recorded and evaluated.

Statistical considerations

The primary endpoint was the prevalence of HCV infection in the study population. The secondary endpoint comprised the characteristics influencing the occurrence of HCV infection in these patients. A descriptive analysis of the variables included in the study was performed, including calculation of frequency distributions for qualitative variables and measures of central tendency and dispersion (mean, standard deviation [SD], and minimum–maximum range) for quantitative variables. The association between HCV infection and categorical variables (i.e., sex, marital status, environment, educational level, legal incapacity status, type of admission and discharge, and mental disorder diagnosis) was assessed by chi-square tests. The influence of continuous variables not following a normal distribution (i.e., age, number of admissions and duration of hospital stay) on the occurrence of HCV infection was analysed using the Mann–Whitney U test due to their high variability.

No imputation was done for missing data and a significance level of 0.05 was used for statistical testing. Statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM Corp., Armonk, NY, USA).

Results

Patients' characteristics

A total of 497 admissions from 345 patients were included. As some patients had been admitted on more than one occasion during the study period, data from the last admission of each patient were considered for the analyses ($n = 345$).

Overall, mean (SD) age was 43.8 (12.1) years. Most patients were women (55.4%). The main diagnoses were schizophrenia spectrum and other psychotic disorders ($n = 185$, 53.6%), followed by depressive disorders ($n = 81$, 23.5%). DD accounted for 21 (6.1%) of the cases. Past history of drug consumption (excluding tobacco) in patients with DD in the overall population included alcohol dependence ($n = 17$), cannabis dependence ($n = 13$), cocaine dependence ($n = 6$), benzodiazepines dependence ($n = 2$), and heroine, amphetamine/methamphetamine and methylenedioxymethamphetamine (MDMA) dependence in one patient each. Socio-demographic and clinical characteristics of patients are summarised in [Table 1](#) and [Table 2](#), respectively.

Table 1 Socio-demographic characteristics (N = 345).

Characteristic	Value
Age (years), mean \pm SD	43.8 \pm 12.1
Gender, n (%)	
Female	191 (55.4)
Marital status, n (%)	
Single	216 (62.6)
Married	60 (17.4)
Separate/divorced	52 (15.1)
Widower	11 (3.2)
In a relationship	6 (1.7)
Environment, n (%)	
Urban	211 (61.2)
Rural	134 (38.8)
Educational level, n (%)	
Illiterate	1 (0.3)
Incomplete primary school	12 (3.5)
Complete primary school	64 (18.6)
Basic education (age 14)	61 (17.7)
Secondary school (age 18)	36 (10.4)
Vocational training	24 (7.0)
Associate degree	19 (5.5)
University degree	47 (13.6)
Unknown	81 (23.5)
Legal incapacity, n (%)	
Yes	28 (8.1)
No	234 (67.8)
Unknown	83 (24.1)

SD: standard deviation.

HCV prevalence

The overall prevalence of HCV infection was 3.8% ($n=13$) and reached 14.3% ($n=3$) among DD patients. Past history of drug consumption (excluding tobacco) in patients with DD and HCV infection included alcohol dependence ($n=3$), cannabis dependence ($n=2$) and cocaine, benzodiazepines, and MDMA dependence in one patient each. The bivariate analyses showed a higher HCV prevalence among patients with DD (14.3% versus 3.1%, $p=0.009$) and with legal incapacity (14.3% versus 1.7%, $p=0.002$) compared to HCV positive individuals without these conditions. As for the continuous variables, the analyses showed a statistically significant relationship between HCV infection and number of admissions, with higher mean (SD) number of hospitalisations in patients with the infection than in uninfected individuals (1.62 [0.87] versus 1.27 [0.66], $p=0.049$, respectively). No significant association was observed between HCV infection and mean (SD) age (uninfected patients 43.8 [12.2] years; infected individuals 42.7 [9.6] years, $p=0.919$) or mean (SD) duration of hospital stay (uninfected patients 71.9 [32.2]; infected individuals 56.0 [31.3] days, $p=0.082$).

HCV antiviral therapy

All patients who tested positive for HCV antibodies ($n=13$) were referred to the Hepatology Unit of the University of

Table 2 Clinical characteristics (N = 345).

Characteristic	Value
Number of admissions, mean \pm SD	1.28 \pm 0.67
Type of admission, n (%)	
Voluntary	231 (67.0)
Involuntary	114 (33.0)
Duration of hospital stay (days), mean \pm SD	71.3 \pm 32.3
Type of discharge, n (%)	
Therapeutic	315 (91.3)
Relocation	11 (3.2)
Voluntary	9 (2.6)
Escape	7 (2.0)
Legal	2 (0.6)
Unknown	1 (0.3)
Diagnosis, n (%)	
Schizophrenia spectrum and other psychotic disorders	185 (53.6)
Depressive disorders	81 (23.5)
Bipolar disorder and related disorders	50 (14.5)
Personality disorders	35 (10.1)
Dual diagnosis	21 (6.1)
Neurodevelopmental disorders	25 (7.2)
Obsessive-compulsive disorders and related disorders	15 (4.3)
Anxiety disorders	9 (2.6)
Somatic symptom disorders and related disorders	5 (1.4)
Eating disorders and food intake disorders	3 (0.9)
Dissociative disorders	1 (0.3)

SD: standard deviation.

Salamanca Health Care Complex. According to their evaluation, 6 patients had detectable HCV RNA with fibrosis scores of F0–F1 ($n=3$), F2 ($n=1$), F3 ($n=1$) and F4 ($n=1$) at diagnosis. All received direct-acting antiviral (DAA) treatment reaching sustained virological response, of which 5 are considered cured, and 1 is still under follow-up with diagnosis of cirrhosis. The rest of the patients ($n=7$) did not comply with adequate follow-up: 3 patients moved, 1 died (not related to HCV) and 3 for unknown reasons.

The analytical data of patients who tested positive for serum anti-HCV upon admission to the Medium-Term In-Patient Psychiatric Unit, transient elastography results and therapeutic data are shown in Table 3. The most frequently used antiviral combination was sofosbuvir and velpatasvir ($n=3$) and all treated patients reached the end of therapy with good adherence achieving sustained virologic response (SVR). Two adverse events (asthenia and headache) were recorded during the treatment, not affecting the treatment, and resolving without consequences.

Other serology results

In the overall sample ($N=345$), 3 patients were identified as HIV positive and 4 tested HBV positive, both infections

Table 3 Data on anti-HCV positive patients (N = 13).

Parameter	Value
<i>Analytical data, median (range)^a</i>	
ALT (U/L)	72.0 (109.0)
AST (U/L)	35.0 (46.0)
GGT (U/L)	55.0 (293.0)
Platelet count (10 ³ /μL)	187.5 (203.0)
HCV-RNA (log ₁₀ IU/L), median (range) ^b	2.99 (4.36)
<i>Transient elastography, n (%)^b</i>	
F0–F1 (<7.6 kPa)	3 (49.9)
F2 (7.6–9.5 kPa)	1 (16.6)
F3 (9.6–12 kPa)	1 (16.6)
F4 (>12 kPa)	1 (16.6)
<i>Treatment, n (%)^b</i>	
Sofosbuvir/velpatasvir	3 (50.0)
Sofosbuvir/daclatasvir	1 (16.6)
Elbasvir/grazoprevir + ribavirin	1 (16.6)
Glecaprevir/pibrentasvir	1 (16.6)

ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: γ-glutamyl transferase; HCV: hepatitis C virus; kPa: kilopascals; RNA: ribonucleic acid; SD: standard deviation.

^a n = 10.

^b n = 6.

previously known. Only one of the HCV positive patients also tested HIV positive. All HIV and HBV patients were derived to the Infectious Diseases Unit for their specific treatment.

Discussion

The higher prevalence of HCV infection in patients with serious mental illness and substance use disorders compared to the general population has been widely reported.^{9,15,16,18} The latest European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) publication on HCV among drug users in Europe states that drug use is the main issue in the health-care burden of the disease, with people who inject drugs being the most affected.¹⁸

Previous studies have mainly focused on outpatient settings. The main finding of the present study is the higher prevalence of HCV infection in a cohort of in-patients with severe mental illness compared to the Spanish general population and its significant increase among patients with DD and legal incapacity. Moreover, we identified a higher number of hospitalisations in patients with HCV infection than in uninfected individuals.

High-risk behaviours are generally associated with mental illness and may contribute to the increased prevalence of HCV infection among these patients. A single-centre Australian study that investigated the change in HCV screening rate in a cohort of 71 psychiatric in-patients comparing prospective testing rates with retrospective data, secondarily assessed the prevalence of HCV infection. Psychotic disorders were the main psychiatric diagnosis (73%) and 50% of patients were injecting drug users. Overall HCV prevalence was 19.7%, which was higher compared to the prevalence observed in the Australian community (1.1%). All patients who tested positive for HCV reported having

injected drugs. Factors associated with HCV seropositivity comparing positive and negative patients were not assessed.¹⁹ Notwithstanding differences in design, and considering that we studied a sample of patients with no past history of intravenous drug use, our results also showed higher overall prevalence of HCV infection in psychiatric in-patients (3.8%) and DD patients (14.3%) compared to the Spanish general population (1.7%).^{6,7} This increased risk of HCV infection has been previously associated with multiple factors, like having multiple sexual partners, poverty or poor access to medical care.²⁰

A subsequent prospective study, conducted in four psychiatric in-patient units in Australia, reported HCV seroprevalence and risk factors associated with infection in a cohort of 260 patients. The main psychiatric diagnosis was major depression (26%), followed by post-traumatic stress disorder (20%) and schizophrenia (19%). Intravenous drug use was reported in 28% of the patients. The HCV seroprevalence was 10.8% (95% confidence interval [95% CI] 7.0–15.0), which was higher compared to the prevalence reported in the Australian community at the time (1.2%–1.8%). Demographic characteristics, primary psychiatric diagnoses and HCV risk factors were compared between HCV positive and negative patients by univariate analysis. Aboriginal ethnicity, schizophrenia, injection drug use, body piercing or tattoos, sexual partners with HCV and exposure to custodial settings were significantly more frequent in seropositive patients. Multivariate analysis showed injection drug use ($p < 0.001$, odds ratio [OR] 44.05, 95% CI 7.9–245.5), age ($p = 0.011$, OR 1.09, 95% CI 1.02–1.16) and exposure to custodial stay ($p = 0.011$, OR 7.34, 95% CI 1.6–33.9) were independent predictors of HCV positivity.²¹ As in our research, this study documented higher rates of HCV infection in psychiatric in-patients compared to the local general population. Although it only involved patients who injected drugs and assessment of HCV seropositivity was limited to the overall sample, substance abuse was also shown to be associated with higher risk of HCV infection.

The literature review on HCV prevalence in psychiatric in-patients in Spain showed few data dating back to 2002. The study involved a retrospective review of the medical records of 332 patients consecutively admitted in an acute psychiatric in-patient unit. The assessed variables included psychiatric diagnosis according to ICD-10 (International Statistical Classification of Diseases and Related Health Problems, 10th revision), history of injecting drug use and HCV serology results. The main psychiatric diagnoses were psychotic and depressive disorders (40.9% and 19.3%, respectively). History of injecting drug use was reported by 6 patients (1.8%). Of the 217 patients in whom serology was requested, 5.1% (95% CI 2.1–8.0) were HCV positive. The associated psychiatric diagnoses were psychotic disorder ($n = 4$), borderline and antisocial personality disorder ($n = 3$), bipolar disorder-manic episode ($n = 2$), depressive disorder ($n = 1$), and adjustment disorder ($n = 1$). In no case was the psychiatric disorder attributed to the infection. Even though this research did not assess the prevalence of HCV infection in drug users nor other characteristics influencing the occurrence of infection, it also demonstrated the higher prevalence of HCV infection in psychiatric in-patients compared to the Spanish urban population, which was estimated at 2% (95% CI 1.1–2.9) in 1996.²² This highlights the

importance of viral screening programmes in psychiatric in-patients, which should include aspects such as psychoeducation, strong patient-psychiatrist relationship, simplified access to treatment and coordination between the Psychiatry and Digestive Units. In addition, it is essential to have a continuous psychosocial approach to these vulnerable patients to ensure proper adherence to the prescribed DAA treatments.^{23,24}

Regarding the higher prevalence of HCV infection in patients with legal incapacity compared to those without this condition, we consider that risk behaviours associated with criminal offences could also occur in the area of personal health. Although we were unable to find studies to compare this result, risk factors among offenders often overlap with those found in psychiatric in-patients, particularly drug abuse and sexual risk-taking behaviour.²⁵

The main limitation of this research is its retrospective nature, which might have led to potential selection and information bias. We also lack information about other risk factors for HCV and about prevalence in drug users in the community, limiting the interpretation of our results. Furthermore, given that this is single-centre study, it is not possible to make inferences beyond the sample population. However, considering that most studies have been performed in acute psychiatric in-patient units and out-patient clinics and the lack of epidemiological research on HCV infection in samples of hospitalised patients with chronic mental disorders and DD, especially in non-intravenous drug users, we show new data in an understudied population. Other strengths include evaluation of the characteristics influencing occurrence of HCV infection in this population, as well as updated information in the Spanish community. In addition, to our knowledge this is the first study evaluating the prevalence of HCV infection in DD and legally incapacitated in-patients.

In conclusion, the prevalence of HCV infection in this large sample of hospitalised patients with severe mental disorders is high compared to the Spanish general population, particularly among patients with DD. These individuals have limited access to health care, and few receive treatment. The presence of a mental illness used to be considered a contraindication for the use of antiviral treatment. In addition, unawareness of HCV infection and polypharmacy could also be barriers to treat patients with severe mental disorders. The availability of treatments with improved efficacy and tolerability,^{16,17} together with the high prevalence of HCV infection in this population indicate that further efforts should be made to include patients with mental disorders, especially those with DD, in HCV screening and treatment.

Ethical considerations

The present work was conducted in accordance with the World Medical Association Declaration of Helsinki, all its amendments, and national regulations. The study was approved by the Ethics Committee for Research with Medicines of the Salamanca Health Area (Salamanca, Spain), and patients were waived from signing the informed consent.

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Conflicts of interest

Carlos Roncero has received fees to give lectures for Janssen-Cilag, Indivior, Servier, GSK, Gilead, MSD, Sanofi, Excelsis, AbbVie, Takeda, Rubio, and Casein. He has received financial compensation for his participation as consultant or as board member of Lundbeck, Gilead, MSD, Mundipharma, Indivior, Excelsis, Camurus, Gebro and AbbVie. He conducted the PROTEUS project, which was funded by a grant from Reckitt-Benckiser/Indivior, as well as the COSTEDOPIA project, which was funded by Indivior. He received two medical education grants by Gilead and medical writing support from AbbVie. Barbara Buch, Ángel Manuel Martín-Sánchez, Ana Isabel Álvarez-Navares, María Pilar Andrés-Olivera, Sinta Gamonal Limcaoco, María Teresa Lozano-López, María Lourdes Aguilar, Felisa Sánchez-Casado and Llanyra García-Ullán declare none.

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