# Combating Hepatitis C in One Psychiatric Facility: An Integrated Approach

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**ABSTRACT** **Background:** The management of chronic hepatitis C virus (HCV) infection in patients with concurrent severe mental illness and substance use disorder poses significant challenges to treatment initiation, adherence, and completion. Multiple barriers impede successful treatment outcomes in this population, including cognitive impairments associated with mental illness, ongoing psychoactive substance use, and inadequate social and environmental support systems.

**Objectives:** To implement a treatment program for HCV-infected patients during their psychiatric hospitalization. To establish a multidisciplinary task force comprising a hepatologist, psychiatric ward team (psychiatrists, nurses, social workers), and a project administrator.

**Methods:** We conducted a retrospective cohort study of patients hospitalized with dual diagnosis (DD) of severe mental illness and substance use disorder who tested positive for HCV antibodies. Patients underwent clinical evaluations and received treatment with direct antiviral agents during hospitalization under the supervision of the joint team. Demographic and clinical characteristics were analyzed.

**Results:** Between January 2018 and June 2023, 694 DD patients were hospitalized, of whom 119 tested positive for HCV antibodies (prevalence 17.1%). Twenty-seven patients (23%) completed treatment; 17 (63%) achieved confirmed sustained virologic response. Treatment discontinuation occurred primarily post-discharge from the mental health facility. Significant efforts were made to engage community caregivers to maintain continuity of care.

**Conclusions:** Our findings demonstrate that treating HCV in patients with concurrent severe mental illness and substance use disorder requires collaborative efforts across medical disciplines. This integrated approach during psychiatric hospitalization provides a unique opportunity for initiating and monitoring HCV treatment in this complex patient population.

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**KEY WORDS:** hepatitis C (HCV), integrated approach, marginal population group, severe mental illness, substance use disorder

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Hepatitis C virus (HCV) infection poses significant health risks, potentially leading to severe complications including hepatobiliary cirrhosis and hepatocellular carcinoma. Beyond liver-specific pathology, HCV infection is associated with increased overall mortality, including deaths not directly attributed to liver disease.

The primary transmission route of HCV involves exposure to contaminated blood through non-sterile equipment, placing individuals with substance use disorder (SUD) at particularly high risk for infection [1]. Within this vulnerable population, patients with dual diagnosis (DD), that is those with concurrent severe mental illness and SUD, face exceptional challenges in managing the disease [2,3]. These patients encounter significant behavioral barriers that impede both their ability to seek and maintain consistent medical care.

DD patients not only face multiple risk factors for HCV infection but may also serve as potential transmission vectors within their communities. This population typically presents with a markedly younger average age compared to other chronic hepatitis C (CHC) patients [4]. Their combination of intensive narcotic use and limited healthcare access amplifies their potential role in disease transmission.

Recognizing these multifaceted barriers, we identified psychiatric hospitalization as a unique window of opportunity to address these challenges effectively and implement comprehensive HCV treatment for this vulnerable population.

## PATIENTS AND METHODS

We performed a retrospective cohort study. The data presented cover the period from 1 January 2018 to 31 May 2023.

The inclusion criteria was hospitalization for severe mental illness (SMI) [5], SUD, and positive HCV antibody test.

Our primary tools for data collection included medical records, specifically digital data and medical files. We employed strict data collection protocols to minimize information bias and ensure data accuracy.

### THE PROCEDURE

The first step of the project was establishing a collaboration between the Hepatology Clinic of the Institute at the Department of Gastroenterology, E. Wolfson Medical Center, and the dual diagnosis ward (DDW) at Abarbanel Mental Health Medical Center, Israel. At the start of the project, the psychiatric team members underwent a comprehensive review of hepatitis C risk factors, epidemiology, diagnosis, and treatment.

We gathered a comprehensive set of data encompassing various aspects of the lives and health status of the participants. The demographic information included age, sex, community support network, living arrangements, history of incarceration. The clinical data included fibrosis stage; serological test results for HCV, hepatitis B virus (HBV), and human immunodeficiency virus (HIV); medical history; current medications; psychiatric diagnoses (according to ICD-10-CM) [6]; and number of previous psychiatric hospitalizations.

According to the project's protocol, all new patients admitted to the DDW underwent screening for HCV, HBV, and HIV infections. HCV positive patients underwent HCV polymerase chain reaction (PCR) to establish viral load and genotype.

Those who tested positive for HCV antibodies but negative for HCV RNA PCR, whether due to prior successful treatment or spontaneous viral clearance, were advised to undergo yearly HCV RNA testing, as recommended by the 2018 European Association for the Study of the Liver (EASL) guidelines on hepatitis C management [7].

Additional blood tests, including CBC and liver function tests (LFTs), were conducted during hospitalization.

We used Fibrosis-4 (FIB-4) [8] as a primary fibrosis risk assessment. For patients with scores below 1.45, indicating a low fibrosis risk, immediate treatment with direct-acting antivirals (DAAs) was recommended. Patients with a FIB-4 score greater than 1.45 underwent liver fibrosis evaluation using FibroScan transient elastography (ECHOSENS®, USA) before recommending treatment. The chosen elastography cutoff values for liver fibrosis stages were stiffness 9 > kPa, 9–12 kPa, and > 12 kPa for no/mild/moderate fibrosis (METAVIR score F0-F1-F2), severe fibrosis (METAVIR score F3), and cirrhosis (METAVIR score F4), respectively. The diagnosis of cirrhosis was based on the transient elastography score (>12 kPa), clinical and imaging data. Patients showing evidence of advanced fibrosis/cirrhosis (F4 on FibroScan) were categorized based on the Child Pugh Classification [9].

The patients were provided with a detailed explanation of the disease and treatment goals. Prior to initiating therapy, we ensured that the mental state of the patients was stable to promote treatment compliance. Most patients agreed to undergo drug treatment.

Before administering DAAs, we assessed potential drug–drug interactions (DDIs) using a web interaction-checker available at www.hepdruginteractions.org. Any changes in co-medications resulting from DDIs were recorded.

DAA in Israel are part of the health fund reimbursements, which means the state pays most of the costs. The drugs were prescribed and approved by the family physician and supplied by health providers, paid either by relatives of the patients or by the *Haverim le Refuah* voluntary association.

The treatment was administered by the nursing staff during the patient's hospitalization. Throughout the treatment period, patients underwent routine clinical and laboratory assessments.

Patients who were discharged from the psychiatric hospital before completing the treatment were referred to the hepatology clinic for further monitoring. Treatment effectiveness was assessed by monitoring for sustained virologic response at 12 weeks (SVR-12), defined as a negative HCV PCR test result, in patients who returned for follow-up outpatient clinic visits. Patients who could not be contacted for more than 18 months were defined as lost to follow-up (LTFU).

We maintained close communication with family physicians, rehabilitation centers, community mental health organizations, and families to ensure effective support and maximize project efficiency.

The study was approved by the local institutional review board.

### STATISTICAL ANALYSIS

All data were collected from the patient's medical files and input to Excel files. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 31 (SPSS, IBM Corp, Armonk, NY, USA). For characterizing the study population, variables are described as frequencies and percentages in each subcategory of nominal and ordinal variables. Quantitative variables were described using mean, standard deviation and range.

## RESULTS

From 1 January 2018 to 31 May 2023, a total of 694 individuals were hospitalized in the DD ward. Among them, 119 (17.1%) tested positive for HCV antibodies. Six (5.1%) were first detected during hospitalization, while the remaining patients had a previous diagnosis [Table 1].

**Table 1.** Demographic, social and clinical determinants of 119 HCV positive patients hospitalized in DDW

| Categorical variable | N (%) |
|---|---|
| Sex: Male | 113 (95.0%) |
| Married | 7 (5.9%) |
| Single/divorced/widowed | 112 (94.1%) |
| Immigrants from the Former Soviet Union | 58 (48.7%) |
| Guardian | 6 (5%) |
| Unemployed | 105 (92.3%) |
| Homeless | 49 (41.1%) |
| Previous incarceration | 89 (74.8%) |
| Alcohol abuse | 61 (51.3%) |
| Active drug users | 77 (64.7%) |
| Opioid agonist treatment* | 61 (51.2%) |
| **Quantitative variables [min-max]** | |
| Age in years | 46.8 ± 9.15 [24–68] |
| Number of previous hospitalizations | 11.22 ± 16.41 [1–85] |

*Methadone/buprenorphine
DDW = dual diagnosis acute ward, HCV = hepatitis C virus

### CLINICAL DIAGNOSTIC FEATURES

#### *Fibrosis severity*

A FIB-4 score was calculated for all 119 patients. In 73 patients (61.3%) Fib-4 was less than 1.45, indicating a low risk for advanced fibrosis. Patients with a medium-risk or high-risk score (n=46, 38.7%) were advised to undergo a FIBROSCAN® assessment. Of these patients, 19 (41.3%) were tested: 11 had low grade fibrosis score (F0-1), one had F3, and seven had F4 fibrosis score. All seven patients with an F4 score had preserved liver function without features of clinically significant portal hypertension (Child Pugh A).

#### *Co-infection*

In total, four patients (3.3%) tested positive for HIV. They were all receiving antiretroviral therapy. In addition, 106 patients (89%) were tested for HBV status [Table 2].

**Table 2.** HBV status of 106 HCV positive patients hospitalized in the dual diagnosis ward

| HBV status | N (%) |
|---|---|
| Susceptible (HBsAg- HBsAb- HBcAb-) | 49 (46.2%) |
| Infected (HBsAg+) | 5 (4.7%) |
| Past infection (HBcAb+) | 43 (40.6%) |
| Immunity (HBsAb+) | 9 (8.5%) |

HBsAg = HB surface antigen, HBsAb = HB surface antibody, HBcAb = HB core antigen, HBV = hepatitis B virus, HCV = hepatitis C virus

Of the total cohort of 119 HCV positive patients, 19 experienced spontaneous clearing; 16 members underwent treatment before psychiatric hospitalization [Table 3].

The remaining 84 patients (70.6%) were recruited for the treatment process [Table 4].

**Table 3.** Common psychiatric diagnosis of 119 hepatitis C virus positive patients hospitalized in the dual diagnosis ward

| Main diagnosis | Value |
|---|---|
| Schizophrenia (F20-F29)* | 61 (51.3%) |
| Anxiety disorders (F40-F48)* | 30 (25.2%) |
| Mental and behavioral disorders due to multiple drug use and use of other psychoactive substances (F19)* | 17 (14.3%) |
| Mood [affective] disorders (F30-F39)* | 11 (9.2%) |

*according to ICD-10

**Table 4.** Treatment outcome of 84 chronic hepatitis C patients treated during hospitalization in the dual diagnosis ward

| Treatment | N (%) |
|---|---|
| Known SVR-12 | 17 (20.2%) |
| Pending SVR-12 | 9 (10.7%) |
| Treatment failure* | 1 (1.2%) |
| Recommended but LTFU for > 18 months | 10 (11.9%) |
| Fully diagnosed but LTFU before treatment | 14 (16.7%) |
| Incomplete laboratory investigation | 26 (30.6%) |
| Refusers | 7 (8.3%) |

*One patient failed treatment twice: once with sofosbuvir/velpatasvir and then with sofosbuvir/velpatasvir/voxilaprevir
LTFU = lost to follow-up, SVR-12 = sustained virologic response at 12 weeks

One patient underwent liver/kidney transplantation followed closely by successful ledispavir/sofosbuvir treatment in 2017, several years before his psychiatric hospitalization. On yearly follow-ups, his HCV PCR remained negative.

Ten patients (8.4%) died at different stages of treatment from non-hepatic causes.

## DISCUSSION

In 2018, a comprehensive initiative was launched to address hepatitis C virus (HCV) infection in individuals with SMI and SUD, aligning with the World Health Assembly's 2016 resolution to eliminate viral hepatitis by 2030. The project's objective was to concurrently investigate the screening, diagnosis, and treatment of CHC in patients experiencing both acute psychiatric conditions and substance abuse.

### DEMOGRAPHY

By the end of the study period, 119 patients had tested positive for HCV Ab. This number corresponded to a 17.1% prevalence of CHC among all individuals hospitalized in the designated department [Table 1]. In contrast, the rate of hepatitis C in the general Israeli population is 2% [3,10]. To provide a comparison, Le et al. [11] reported a CHC rate of 8% among psychiatric inpatients in an academic-affiliated tertiary referral medical center in Northern California, compared to 1–1.7% in the general population. Girardin and colleagues [4] showed a prevalence of 25.7% of CHC in a Swiss cohort of psychiatric inpatients, while the national prevalence in the general population is approximately 0.5%.

Our study shows that immigrants from the former Soviet Union (FSU) account for almost half of the cohort. The causes for such prevalence include higher incidence of HCV in the overall FSU Israeli population due to an extended use of non-sterile medical equipment and a high prevalence of injection drug use [10]. Having same-language-speaking caregivers on our team proved to be an advantage that improved communication and built easier trust with patients.

The demographic characteristics of the sampled study show a marginal population very different in its characteristics from the general population: 41% are street dwellers, compared to less than 0,04% of the general population in Israel [12], 78.2% had a criminal record compared to 3.1% of the general population [13], 86.3%, were unemployed, compared to an average of 2.7% of the general population in Israel in the years in which the study was conducted [14].

Only seven individuals were married, and six had legal guardians, indicating a low level of social support.

In our sample of SMI patients, schizophrenia was the most common diagnosis at 51.2%. Anxiety disorders (25.2%) and psychotic disorders due to psychoactive substances (14.3%) were also prevalent. A high percentage of patients had personality disorders, 14.3% in the sample compared to 7.8% in the general population [15].

Moreover, 61 patients (51.2%) had a history of alcohol abuse, which is strongly linked to liver damage [16]. As a result, patients may have faced additional challenges in treatment due to compromised liver function, complicating both medical interventions and recovery outcomes.

### FIBROSIS ASSESSMENT

We found that 38.7% of patients had intermediate to high risk of liver fibrosis based on FIB-4 scores, compared to the global average of 25% [17]. While FIBROSCAN® evaluation was intended for all patients with FIB-4 scores above 1.45, we were unable to complete this comprehensive assessment in all cases. Among those who underwent FIBROSCAN® testing, most showed minimal fibrosis (stage 0–1). However, eight patients were diagnosed with advanced fibrosis, including seven with stage 4 cirrhosis. None of these eight patients remained in care.

### VIRAL COINFECTION

Individuals with HCV infection are at high risk of HIV and hepatitis B due to similar infection routes and risk factors. Four patients were HIV-positive and on antiretroviral therapy.

The EASL guidelines state that HBV–HCV co-infection prevalence in Europe and North America is usually 1-5% but can rise in populations with overlapping risk factors, such as injection drug users or HIV-positive individuals [7]. The rate of co-infection with HBV in the current study was 4.7%; 40.6% of patients showed evidence of past infection.

Despite official guidelines advocating for immunization in this patient group, only 8.5% of our cohort had received the HBV vaccine. This alarmingly low rate underscores the significant gap in hepatitis B vaccination coverage among this vulnerable population, indicating a critical need for improved immunization strategies and awareness [18].

### TREATMENT SUCCESS

Of 119 diagnosed patients, 7 (8.3%) refused to continue treatment; 84 were eligible for treatment.

Research has shown high effectiveness of DAAs. The main condition for achieving the goal was keeping an uninterrupted treatment sequence. All 27 patients (32.1%) who started treatment finished the whole process. Most patients (70.3%) were treated with sofosbuvir/velpatasvir and the rest with glecaprevir/pibrentasvir (29.7%). The treatment decision was based on DDI concerns. No significant adverse effects were observed. There was no need to change psychiatric treatment to proceed with antiviral therapy. Treatment failure occurred with one patient who was treated with two courses of antiviral therapy: first with

sofosbuvir/velpatasvir and then with sofosbuvir/velpatasvir/voxilaprevir. This patient was hospitalized during both treatment courses, securing his compliance. We did not search for viral mutations for this patient, so we have no clear explanation for the reason for the failure.

Patient retention was complicated by the revolving door phenomenon, often requiring multiple hospitalizations to complete treatment. Patients who were unreachable for more than 18 months, were defined as LTFU.

A total of 50 patients were LTFU between the data collection phase and the preparation of this article. A group of 10 patients was LTFU after receiving prescriptions, possibly due to brief hospital stays, 14 patients were fully diagnosed but became LTFU before initiating treatment, and 26 patients only underwent incomplete laboratory investigations.

The limitations of the study include its retrospective design, the single-center approach, which was limited to a specific region of Israel, and the absence of a control group. Additional multicenter prospective studies are needed to investigate and improve the accessibility of HCV treatment for these complex patients.

## CONCLUSIONS

The complex needs of patients with DD of addiction and mental illness, coupled with HCV infection, necessitate close collaboration between mental health services and general medical settings. Establishing cooperation among liver specialists, psychiatrists, family doctors, and social services highlights both the challenges and benefits of this integrative approach. Numerous bureaucratic and therapeutic obstacles emerged, such as coordinating treatment and follow-up between different services and transferring relevant medical information while upholding confidentiality standards. However, through joint efforts, typical barriers to accessing services for this underserved population can be overcome, including the coordination of tests and adjustments to drug treatments for complex physical and mental conditions.

Looking ahead, the model tested in this project could serve as a foundation for formal protocols that establish routine collaboration and information sharing among various care providers, integrating it into the standard of care for patients with chronic physical and mental illnesses.

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