

Depression and anxiety in patients with hepatitis C: prevalence, detection rates and risk factors

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Abstract

Objective: We examined a group of patients awaiting interferon treatment for hepatitis C to estimate the prevalence and detection rates of and risk factors for mood disorders.

Methods: The Structured Clinical Interview for *DSM-IV* Axis I Disorders: Clinician Version was used to detect psychiatric disorder. Self-completion instruments were used to rate symptom severity, subjective cognitive function, work and social adjustment, stigma, acceptance of illness and treatment satisfaction.

Results: The 90 participants included 23 women (26%); 33 (37%) had contracted hepatitis C iatrogenically, 42 (47%) through injecting drug use and the remainder (17%) were of unknown origin. There was a 28% 1-month prevalence of depressive disorders, 72% of whom were previously undiagnosed, and a 24% prevalence of anxiety disorders, 86% previously undiagnosed. Current methadone maintenance was strongly associated with risk of depression (odds ratio, 5.0; 95% CI, 1.08–23.0). After adjustment for age and sex, depression was associated with poorer work and social adjustment, lower acceptance of illness, higher illness stigma, poorer reported thinking and concentration, and higher levels of subjective physical symptoms (all $P < .05$). Anxiety disorders were uncorrelated with any risk factor.

Conclusions: Depression and anxiety have high prevalences in hepatitis C, and are largely undetected and treated. Depression, but not anxiety, is associated with adverse experiences of illness.

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1. Introduction

Hepatitis C poses a very significant health problem on a global scale [1]. The World Health Organization estimates that 3% of the world's population (170 million people) is infected with hepatitis C virus [2] and is at risk of developing liver cirrhosis and liver cancer. Hepatitis C is now the leading cause of end-stage liver failure and the leading indication for liver transplant in the developed world.

Like many chronic medical illnesses, hepatitis C is associated with an increased prevalence of psychiatric disorder [3,4], particularly depression. The presence of depressive symptoms in hepatitis C, as in other chronic

medical illnesses, is important because they have an adverse effect on the course of illness, with amplification of physical symptoms, functional impairment, reduced treatment compliance and reduced quality of life [5]. The association is also of particular importance in hepatitis C because patients often come from population groups at risk for psychiatric disorder, such as injecting drug users (IDUs). In addition, treatment for hepatitis C involves interferon alfa, which has neuropsychiatric side effects. Psychiatric disorder is the main reason for delay or discontinuation of interferon alfa treatment [6]. Successful medical treatment of hepatitis C therefore requires detection and management of depression both before and during treatment [5].

The reasons for the high prevalence of depression in persons with hepatitis C are not clear; these have been hypothesized to arise from the disease itself, or from the high proportion of persons at risk for psychiatric disorder among

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those affected by hepatitis C, or to the stigmatizing nature of the diagnosis.

Studies of psychiatric symptoms in hepatitis C have frequently relied on self-administered scales rather than a formal psychiatric assessment, making it difficult to assess the clinical significance of their findings. They have also tended to focus on depression and omit anxiety disorders. Finally, studies have for the most part reported on the prevalence of psychiatric disorder without making the important distinction between previously diagnosed and hitherto-unrecognized disorder.

In this study we examined a group of patients with hepatitis C awaiting interferon treatment to estimate the prevalence of psychiatric disorder and to identify factors associated with increased risk of depression and anxiety disorders. We examined two types of risk factor of mood disorder: (a) *clinical variables* related to the disease itself, such as route of infection and comorbidity (in particular, HIV), and (b) variables that measure the patient's *experience of illness*, such as acceptance of illness, work and social adjustment, and illness-related stigma.

2. Methods

2.1. Participants

Participants were recruited from patients scheduled for interferon treatment for hepatitis C attending outpatient clinics at St James's Hospital, a university teaching hospital serving a predominantly deprived area of inner-city Dublin. Such patients would have fibrosis grades 2–6 in the absence of cirrhosis. Potential participants were excluded if they were unable to be interviewed because of language or cognitive difficulties. Participants who were incarcerated at the time of hospital visit were only interviewed if in the opinion of accompanying prison staff this could be done in private without either the risk of harm to the interviewer or of the patient using the interview as a means of absconding. The study was approved by the Research Ethics Committee of St James's Hospital. Participants whose assessment revealed untreated psychiatric disorder were offered a referral to the relevant psychiatric services. Written informed consent to participate was obtained from all participants.

2.2. Measures

Participants were interviewed by the first author, a senior registrar in psychiatry, using the Structured Clinical Interview for *DSM-IV* Axis I Disorders: Clinician Version (SCID-CV) [7], which has been designed for use in clinical settings with either psychiatric or general medical patients. Diagnostic interviews were carried out blind to the results of the self-administered measures. Using SCID-CV criteria, current psychiatric diagnosis was based upon symptoms reaching caseness level at the time of interview or in the preceding month. Lifetime diagnosis was based on the

occurrence of symptoms reaching caseness level prior to the month preceding interview. Alcohol misuse was based on the diagnosis of either alcohol abuse or alcohol dependence syndrome.

Self-administered measures were used to assess factors associated with risk. We used a scale developed by Fife and Wright [8] to assess experience of illness-related stigma within the previous month. This measure has 23 items and comprises four dimensions of social rejection, financial stigma, internalized shame and social isolation. Work and social adjustment was measured using the WSAS, a short scale developed by Marks [9]. Mundt et al. [10] report that the scale has high internal consistency and is sensitive to differences between patients in disorder severity and to treatment-related change within patients. Acceptance of illness was measured using Felton's eight-item scale [11,12], which assesses the extent to which respondents are able to accept their illness without experiencing negative feelings or responses. We devised simple self-rating scales to assess frequency and severity of hepatitis C symptoms within the 2 weeks prior to assessment, and subjective impairment of thinking and concentration.

2.3. Analysis

Data were analyzed with Stata Release 8.2. Confidence intervals for proportions were calculated using Wilson's method. Relationships between risk factors and psychiatric disorder are expressed as odds ratios. The relationship between risk factors and the presence of either anxiety or depressive disorders was calculated using multinomial logistic regression. This allows the assessment of how each risk factor affects the probability of each of the two disorders relative to the probability of neither disorder.

Because the scales assessing perception and experience of illness are all scored on different, arbitrary scales, these scores were reexpressed a quartile of the score distribution of the test for ease of interpretation and comparison of the effects of each scale.

3. Results

3.1. Participant characteristics

A total of 101 potential participants were identified. Of these, five declined to participate. A further six were currently incarcerated and regarded as too high a security risk to be allowed to be interviewed in private. Table 1 shows the characteristics of the 90 participants who form the study sample.

A quarter of participants were women. Compared with men, the women were significantly older, with a median age of 44 years compared with a median age of 37 years in the men ($P=.004$). A significant proportion of the participants had iatrogenic hepatitis C. Ten of the 13 women with iatrogenic disease had acquired it through contaminated anti-D immunoglobulin and three from transfusions. Fifteen

Table 1
Characteristics of the participants

	Women	Men	Total
Route of infection	23 (25.6%)	67 (74.4%)	90 <i>P</i> = .047 ^a
Unknown	4 (17.4%)	11 (16.4%)	15 (16.7%)
Iatrogenic	13 (56.5%)	20 (29.8%)	33 (36.7%)
Injecting drug use	6 (26.1%)	36 (53.7%)	42 (46.7%)
Age			<i>P</i> = .004 ^b
Median (25th/75th percentile)	44 (35/49)	37 (32.5/41)	38 (33/44)
Social class (<i>n</i> = 85)			<i>P</i> = .120 ^a
Nonmanual (A, B and C1)	14 (60.9%)	26 (41.9%)	40 47.1%
Marital status			<i>P</i> = .554 ^a
Living with partner/spouse	15 (65.2%)	39 (58.2%)	54 (60.0%)
HIV status			<i>P</i> = .278 ^a
Positive	7 (30.4%)	29 (43.3%)	36 (40.0%)

One woman had contracted hepatitis C sexually, which was not shown in the table.

^a χ^2 Test.

^b Wilcoxon rank sum test.

of 20 men with iatrogenic disease had acquired it through contaminated blood products for treatment of hemophilia and a further five through transfusion. Women were more likely to have iatrogenic hepatitis C (56% of women) than men, in whom the commonest route of infection was injecting drug use (54%). There was a similar proportion of cases of unknown etiology in the two sexes (17%). Social class based on occupation (or occupation of head of household where the participant was a housewife or long-term unemployed) was classifiable in 85 persons. Just under half of participants were in the nonmanual classes (A, B and C1). Sixty percent of participants were living with partners or spouses. Forty percent of participants were HIV-positive. There was a significant relationship between route of infection and HIV comorbidity, with 57% of the IDU participants being HIV-positive (*P* = .006, χ^2 test) compared

with five persons (33%) among those with unknown etiology and seven (21%) among those with iatrogenic infection. All seven were men with hemophilia.

3.2. Prevalence of current and lifetime psychiatric disorder

There were no participants who met the criteria for psychotic or eating disorders, current or lifetime.

3.2.1. Depressive and anxiety disorders

Table 2 shows the prevalence of depression and anxiety disorders on clinical interview using the SCID-CV. There was a 28% 1-month prevalence of depressive disorder. Prevalence was higher in women (44%) than in men (22%), although this difference was of borderline statistical significance (*P* = .051). Among those with depressive disorder, the commonest diagnosis was of adjustment disorder with depressed mood (with or without anxiety), which occurred in 10 of 25 participants. There were seven participants who met the criteria for major depressive disorder (8%) with the remaining eight receiving diagnoses of dysthymia or depressive disorder not otherwise specified. Twenty-two participants (24%) had anxiety disorders, with a similar prevalence in both sexes. The commonest anxiety disorders were panic and phobic disorders, which accounted for half of the diagnoses. There were eight participants (9%) who met the criteria for both depressive disorder and anxiety disorder. The prevalence of coexisting anxiety and depressive disorders was significantly higher in women (22%) than in men (4.5%; *P* = .012). There was no statistical association between the presence of depressive and anxiety disorders (χ^2 test, *P* = .301).

Thirty-two participants had a lifetime diagnosis of depressive disorder (36%). Of these, 14 were currently depressed. Forty-five participants (50%), in total, had, therefore, either a current or lifetime diagnosis of depressive

Table 2
Depression and anxiety disorders diagnosed using the SCID-CV

	Women	Men	Total
Depression: current			<i>P</i> = .051 ^a
<i>n</i> (%) (95% CI) ^b	10 (43.5%) (25.6–63.1%)	15 (22.4%) (14.1–33.7%)	25 (27.8%) (19.6–37.8%)
Major depressive disorder	3	4	7 (7.8%) (3.8–15.2%)
Adjustment disorder with depressed mood	6	4	10 (11.1%) (6.1–19.3%)
Depressive disorder NOS or dysthymia	1	7	8 (8.9%) (4.6–16.6%)
Depression: lifetime			<i>P</i> = .154
<i>n</i> (%) (95% CI)	11 (47.8%) (29.2–67.0%)	21 (31.3%) (21.5–43.2%)	32 (35.6%) (26.4–45.8%)
Anxiety: current			<i>P</i> = .181 ^a
<i>n</i> (%) (95% CI)	8 (34.8%) (18.8–55.1%)	14 (20.9%) (12.9–32.1%)	22 (24.4%) (16.7–34.2%)
Adjustment disorder with anxiety	4	2	6 (6.7%) (3.1–13.8%)
Panic disorders and phobias	3	8	11 (12.2%) (7.0–20.6%)
Anxiety disorder NOS	1	2	3 (3.3%) (1.1–9.3%)
Obsessive–compulsive disorder	0	2	2 (2.2%) (0.6–7.7%)
Anxiety: lifetime			<i>P</i> = .398 ^a
<i>n</i> (%) (95% CI)	6 (26.1%) (12.5–46.4%)	12 (17.9%) (10.6–28.7%)	18 (20.0%) (13.0–29.4%)
Comorbid depression and anxiety			<i>P</i> = .024 ^c
<i>n</i> (%) (95% CI)	5 (21.7%) (9.7–41.9%)	3 (4.5%) (1.5–12.4%)	8 (8.9%) (4.6–16.6%)

^a χ^2 Test.

^b Binomial confidence intervals calculated using Wilson's method [13].

^c Fisher's Exact Test.

Table 3
Alcohol and substance misuse diagnosed using the SCID-CV

	Women	Men	Total
Alcohol abuse or dependence			$P=.002^a$
<i>n</i> (%) (95% CI) ^b	2 (8.7%) (2.4–26.8%)	23 (34.3%) (24.1–46.3%)	25 (27.8%) (19.6–37.8%)
Current	1 (4.0%) (0.8–21.0%)	0 (0–5.4%)	1 (1.1%) (0.2–6.0%)
Lifetime	1 (4.0%) (0.8–21.0%)	23 (34.3%) (24.1–46.2%)	24 (26.7%) (18.6–36.6%)
Opiate abuse or dependence			$P=.039^a$
<i>n</i> (%) (95% CI) ^b	5 (21.7%) (9.7–41.9%)	35 (52.2%) (40.5–63.7%)	40 (44.4%) (34.6–54.7%)
Current	3 (13.0%)	20 (29.8%) (20.2–41.7%)	23 (25.6%) (17.7–35/4%)
Lifetime	2 (8.7%) (2.4–26.8%)	15 (22.4%) (14.1–33.7%)	17 (18.9%) (12.1–28.2%)

^a Fisher's Exact Test.

^b Calculated using Wilson's method.

disorder. Eighteen participants had a lifetime diagnosis of anxiety disorder (20%) of whom only four had a current anxiety disorder diagnosis. A total of 36 participants (40%) had either a current or lifetime diagnosis of anxiety disorder.

3.2.2. Detection of depression and anxiety

Of the 25 participants who received a diagnoses of current depressive disorder on the SCID-CV, 18 (72%; 95% CI, 52–86%) were detected for the first time by the study interview; five others had been previously assessed for depression by their general practitioner and two by a psychiatrist. All seven of those assessed had been started on treatment. In five cases, treatment was with drug therapy and in two cases the person had been sent for counseling or psychotherapy. In five of the 18 participants whose depression had not been assessed formally, concern had been expressed at some point by either relatives or hospital staff, and this concern noted in the chart. There were 45 participants who had either a current or lifetime diagnosis of depressive disorder. Of these, 23 (51.1%; 95% CI, 37–65%) had never been formally evaluated and only four (8.9%; 95% CI, 3.5–21%) had been evaluated by a psychiatrist.

The 22 participants with a current anxiety diagnosis had a lower rate of detection and treatment with 19 (86%; 95% CI, 67–95%) detected for the first time while participating in the study. The remaining three had been assessed formally, two by a general practitioner and one, who had obsessive–compulsive disorder, by a psychiatrist. All were on drug treatment. One further participant had been assessed for a previous anxiety disorder. Detection rates were lower still when current and lifetime anxiety disorders were considered. Of 33 participants who had either a current or lifetime diagnosis of anxiety disorder, only the three patients referred to above had been evaluated formally, with the remaining 30 (91%; 95% CI, 76–97%) undetected and untreated.

3.2.3. Alcohol and substance misuse

Table 3 shows the prevalence of abuse or dependence involving alcohol or opiates. While only one participant met the criteria for current misuse of alcohol, a quarter of participants met the lifetime criteria (26.7%). All but two of those meeting the criteria for alcohol abuse or dependence were men ($P=.002$). Forty participants (44.4%) met the criteria for opiate misuse, either current (25.6%) or lifetime (18.9%). All but one participant who met the criteria for opiate misuse were receiving methadone maintenance therapy. There was also a higher prevalence of opiate misuse in men than in women ($P=.039$). The prevalence of alcohol misuse, current or lifetime, was similar in those who had contracted hepatitis C by injecting drug use (15 persons, 35%) and in those whose etiology was unknown (5 persons, 33%). Although it was lower in those who had iatrogenic hepatitis C (5 persons, 15%), the variation in prevalence between the groups was not statistically significant ($P=.298$, χ^2 test).

3.3. Factors associated with depression

3.3.1. Demographic and disease-related factors

We examined demographic and disease-related factors for associations with depression. These are summarized in Table 4.

Risk of depression was higher in women than in men (odds ratio, 2.9) and increased with age. Compared with participants whose hepatitis C was of unknown etiology, there was no significant increase in risk of depression associated with either infection acquired either iatrogenically or by injecting drug use, and when age, sex and current methadone maintenance were controlled for, the odds ratio associated with each route of infection was close to unity. Current methadone maintenance emerged as the strongest predictor of depression, with an adjusted odds ratio of 5.

Comorbid HIV infection was not associated with depression with an odds ratio of 1.4 (95% CI, 0.5–3.8) when corrected for age and sex. Only one of the 15 men who had acquired hepatitis C by treatment for hemophilia had a diagnosis of depressive disorder, and although the

Table 4
Predictors of depressive disorder diagnosed using the SCID-CV

	Unadjusted odds ratio (95% CI)	Adjusted odds ratio ^a (95% CI)
Female sex	2.7 (0.98–7.3)	2.9 (0.91–9.2)
Age (10-year increase)	1.7 (0.94–3.2)	2.0 (0.96–4.0)
Route of infection		
Unknown (baseline)	1.0	1.0
Iatrogenic	1.5 (0.34–6.6)	0.99 (0.20–4.9)
Injecting drug use	1.8 (0.43–7.4)	1.02 (0.16–6.3)
Current methadone treatment	2.7 (0.98–7.3)	5.0 (1.08–23.0)

Odds ratios calculated from logistic regression.

^a Based on all factors shown in the table.

odds ratio, corrected for age, was 0.2, the confidence interval was wide (0.02–1.6) and the association not statistically significant ($P=.128$).

We also examined these factors for association with anxiety disorders, diagnosed by the SCID-CV. There were no significant univariate or multivariate associations.

3.3.2. Experience and perception of illness and risk of depression

Table 5 shows the relationship between depression and experience and perception of illness. Adjusted for age, sex and current methadone maintenance, risk of depression was associated with both the frequency of physical symptoms and their rated impact on daily life, in each case with an odds ratio of approximately 2 associated with a change of one quartile in scale score, although in the case of the impact of symptoms on daily life, the confidence interval included unity. Likewise, work and social adjustment scale scores showed an odds ratio of 2.4 per quartile change. Poorer acceptance of illness was associated with an increased risk of depression, although the confidence interval spanned unity. Both self-rated impairment of memory and concentration were also significantly associated with depression. Illness-related stigma was linked with risk of depression, with an odds ratio of 2.1 per quartile increase in score.

We also examined these factors as potential risk factors for anxiety disorders. Because of the possibility that comparing those with anxiety disorders to the remainder of the participants would cause confounding, due to the positive association between depression and the predictors, we used a multinomial logit model, in which the two outcomes simultaneously modeled were (a) depression and (b) anxiety in the absence of depression. This analysis resulted in the risk factor associations shown in Table 5 being confirmed for depression. No significant risk factors for anxiety disorders, however, emerged from the analysis. Because of the small numbers of participants with comorbid anxiety and depression, we were unable to examine specific risk factors for this group with any degree of precision. The

risk factor associations were, however, similar to those for depression alone.

4. Discussion

4.1. Prevalence of psychiatric disorder

In common with persons with other significant medical illnesses [14], persons with hepatitis C have high rates of psychological symptoms and reduced quality of life compared with the general population [3,15–21]. Kenny-Walsh [22] reported a 16% prevalence of depressed mood noted in the medical charts of 376 Irish women with iatrogenic hepatitis C. Lee et al. [23] reported a prevalence of 24% for depression in 500 patients seen at a tertiary referral center, and Dwight et al. [5], using a standardized psychiatric interview, found a 28% prevalence in 50 patients. However, most studies (including the present one) have been based at tertiary referral centers, making it difficult to determine the applicability of the research to the general population. And while there is broad agreement as to the high prevalence of psychiatric disorders in persons with hepatitis C, there has been a wide variation in the methods of ascertainment used, ranging from self-report and chart review through self-completion measures to formal psychiatric interview. It should be noted, however, that despite this variability in methods, most studies report prevalences of 20–30% for depression.

In common with the studies cited above, we found significant levels of depression in persons with hepatitis C. The prevalence of 28% in our sample agrees well with that reported by other studies that used standardized psychiatric interview [5,24,25].

While there have been numerous studies of depression in persons with hepatitis C, few studies have addressed the problem of anxiety disorders. This reflects a general neglect of anxiety among medical patients in the research literature [26]. Anxiety, where it has been assessed, has frequently been based on self-completion instruments in which the relationship between “caseness” and the clinical diagnosis of an anxiety disorder is unclear. Available data on the prevalence of anxiety disorders in persons with hepatitis C indicate that the prevalence is at least as high as that of depressive disorders [20,21,27–31].

The prevalence of 24% which we found is similar to that of depressive disorder. Furthermore, the use of the SCID-CV, which is based on *DSM-IV* diagnostic criteria, may understate the prevalence of anxiety disorders [32]. The *DSM-IV* classification of anxiety disorder has been criticized for applying a hierarchical system in which anxiety disorders are excluded from diagnosis if they occur in the presence of a depressive episode.

There was also a high prevalence of alcohol abuse or dependence. It should be noted that the prevalence of current alcohol abuse or dependence almost certainly is an underestimate. All participants were candidates for interfer-

Table 5
Illness-related predictors of depressive disorder diagnosed using the SCID-CV

Self-rated ^a	Odds ratio ^b per quartile increase (95% CI)
Symptom frequency	2.0 (1.2–3.3)
Symptom impact in daily life	1.7 (0.98–2.9)
Work and social adjustment	2.4 (1.4–4.3)
Acceptance of illness	1.6 (0.93–2.7)
Impairment of memory	2.3 (1.4–3.9)
Impairment of concentration	3.7 (1.9–3.7)
Illness-related stigma	1.9 (1.1–3.3)

Odds ratios calculated from logistic regression.

^a In all cases, higher quantiles indicate greater burden.

^b Odds ratios are adjusted for age, sex and current methadone maintenance.

on therapy and may have been unwilling to disclose current alcohol misuse for fear that it would prejudice their chances of being treated.

4.2. *Detection of psychiatric disorders*

Despite the considerable literature on the prevalence of mood disorders in persons with hepatitis C, few studies have distinguished between previously recognized and hitherto-unrecognized mood disorder. However, there is a consensus that depression and anxiety in medical patients is frequently unrecognized, undiagnosed and untreated [14,26]. Beausang and Syed [33], Hansen et al. [34] and Vaeroy et al. [35] report recent findings in hospital inpatients indicating that undetected mood disorder continues to be a significant problem in medical patients.

In our study, the great majority of persons with mood disorders had never received an evaluation of their symptoms or received treatment. Almost three quarters of those with a depressive diagnosis, and 90% of those with an anxiety diagnosis, had received no formal psychiatric evaluation, even at general practitioner level, despite their prolonged contact with the medical services. The detection of anxiety disorders was particularly poor. While patient medical charts occasionally contained a note expressing concern that the patient might be depressed, no comments related to anxiety symptoms were recorded in medical notes.

There may be several factors contributing to this widespread failure to detect and manage mood disorders in this patient group. First, psychiatric disorders are seen as stigmatizing, and there may be a reluctance on the part of the medical staff to involve psychiatric services in the management of hepatitis because of the fear of increasing the person's sense of stigma. It should be remembered, however, that most persons with hepatitis C are medically well, and that the most significant factor threatening their quality of life is the high prevalence of psychiatric disorder. Failure to manage these disorders appropriately will have a significant impact on the well-being of this patient population. Second, studies of satisfaction with medical services among persons affected by hepatitis C suggest that there may be also a component of institutionalized stigmatization by the medical staff [36,37] leading to a higher threshold for psychiatric intervention. It is possible, too, that medical professionals' treatment priorities diverge significantly from those of patients [38], leading to an emphasis on physical disease on the part of the doctor while the patient is more concerned about quality of life. Finally, the medical staff is inclined to view depression and anxiety as "natural" in people who are medically ill, thereby depriving them of the potential benefits of treatment [39].

4.3. *Predictors of depression and anxiety*

While numerous studies have found high levels of psychiatric morbidity in persons with hepatitis C, the reasons for these are the subject of considerable debate.

There are three broad classes of hypothesis put forward. Some authors have postulated that the disease process involved in hepatitis C gives rise to psychiatric morbidity. Others have rightly pointed out that persons with hepatitis C come from population subgroups who carry a high risk of psychiatric disorder. Finally, a third line of reasoning has suggested that disease labeling, with the stigma that this entails, is responsible for the increased rates of morbidity.

One of the limitations of the current study was the fact that there was no clinically important variation between patients in their disease severity; as candidates for interferon therapy, all patients would have fibrosis grades 2–6 in the absence of cirrhosis. We were therefore unable to investigate any links between disease severity or progression and either depression or anxiety, which has been the subject of a number of studies. Nevertheless, it is worth noting that in a review of this literature in 2002, Wessely and Pariante [40] concluded that "although there are elegant theoretical mechanisms, there is no compelling epidemiological evidence for an additional HCV specific fatigue or depression factor."

The second hypothesis has argued that the elevated levels of psychiatric morbidity seen in hepatitis C are due to the high levels in the population subgroups in which hepatitis C tends to occur. The group most at risk of hepatitis C, current and former IDUs, has an increased risk of psychiatric disorder independent of hepatitis C status, both due to their sociodemographic characteristics and to the high prevalence of antisocial personality disorder which is a risk factor for both mood disorder and for hepatitis C [41]. Several studies of IDUs have shown that prevalence of psychiatric disorder is similar in those with and without hepatitis C infection [42,43]. It is notable in our study that persons with iatrogenic hepatitis C had levels of mood disorder similar to those in participants who had contracted the disease by injecting drug misuse. While the sociodemographic characteristics of the hepatitis C population may account for some of the excess psychiatric morbidity observed, there are clearly other factors also at work.

One important subgroup at greatly increased risk of depression comprised participants on methadone maintenance. These had a fivefold increase in risk of depressive disorder. Similar findings have been reported by Brienza et al. [44] and Mason et al. [45], and is in line with the general finding of elevated rates of psychiatric disorders in opiate misusers [46]. In particular, the prevalence of psychiatric disorder is up to 10 times higher in persons on methadone maintenance than in the general population and is two to three times higher than that found in community surveys of those with a substance-use disorder [47]. This may reflect a general tendency, observed by Galbaud du Fort et al. [48], over a wide range of disorders for persons with a comorbid anxiety or depressive disorder to have a higher probability of seeking treatment. While the reasons for this are still a matter of debate, it underlines the need for psychiatric assessment in this vulnerable subgroup.

The third set of hypotheses proposes that the stigma involved in the diagnosis of hepatitis C is central to the reduced psychological well-being found in patients. Córdoba et al. [49] has argued on the basis of his research [16] that the process of labeling involved in the diagnosis may be the key factor in the high levels of distress. In support of this, the findings of Coughlan et al. [17] that the rates of depression were similar in those who had chronic hepatitis C as in those who had evidence of previous acute infection reported above, only suggest strongly the importance of the process of diagnosis itself. Corroborative findings were reported by Rodger et al. [19] in a study of former intravenous drug users; those who were aware of their HCV-positive serostatus reported more depression than people with comparable liver disease who were unaware of their diagnosis.

Our results confirm the importance of experience of illness as predictors of depression. In particular, illness-related stigma, acceptance of illness, work and social adjustment, and self-rated frequency and impact of symptoms were all associated with increased risk.

Several limitations of the current study must be borne in mind. The limited sample size may have allowed significant associations to go undetected. Second, the sample was drawn from a relatively homogenous group of patients attending a single hospital. However, in view of the broad agreement between our findings and those in other tertiary referral centers, it is unlikely that the sample is untypical or that the results contain important biases.

It should be borne in mind that this is a cross-sectional study. For this reason, the direction of association between some of the risk factors and depression may be in either direction. For example, it may be that those who are most stigmatized are most vulnerable to depression, or it may be that a sense of stigma is heightened by the cognitive distortions of depression. Longitudinal research will be needed to clarify such associations.

As noted earlier, this was a clinically homogeneous group without significant medical comorbidity aside from HIV infection. As a result, we were unable to explore relations between these factors and psychiatric disorder. Finally, we should point out that the assessment of current alcohol use is probably biased by the circumstances of the study. Patients may have believed that their chances of obtaining interferon treatment would be compromised by revealing current alcohol abuse.

5. Conclusions

Our study underlines the significant prevalence of undiagnosed mood disorder in persons with hepatitis C, with significant levels of psychiatric disorder across all patient subgroups. It also corroborates a growing literature linking illness-related variables to well-being in hepatitis C. These findings, taken together, suggest that the management of the hepatitis C, while taking liver function into account, must be

more broadly based in order to achieve maximum quality of life and function in patients. All those affected must be seen as at risk of psychiatric disorder, and management aimed at offering the best quality of life must include a component of evaluation and management of psychiatric symptoms.

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