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CRITICAL REVIEW

Alcohol misuse in patients with alcohol-related liver disease: How can we do better? A narrative review of the literature

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Abstract

Background: Ongoing alcohol use is strongly associated with progressive liver damage and higher mortality in patients with alcohol-related liver disease (ArLD). Reduction in alcohol use is therefore the cornerstone of treatment to improve the long-term outcome of these patients. However, a large proportion of patients continue to use alcohol and do not access or engage with alcohol treatment services after a diagnosis of ArLD. We reviewed the literature on factors associated with ongoing alcohol consumption among patients with ArLD to identify barriers or facilitators to their accessing alcohol treatment.

Methods: A search of MEDLINE and EMBASE was conducted using search strategies relating to ArLD and the psychosocial factors hypothesized to influence alcohol reduction and/or abstinence.

Results: There were few relevant studies pertinent to this population group. Several studies reported a high prevalence of mental health diagnoses associated with the severity of alcohol dependence. Social and environmental factors were shown to be important determinants of alcohol use. Common themes perceived as barriers to treatment from qualitative interviews with ArLD patients across studies included poor communication between the clinical team and patient, lack of symptoms recognized by patients themselves, and perceived loss of control over their condition.

Conclusions: We recommend that future clinical studies of patient cohorts with ArLD include detailed psychosocial assessments to capture information on mental health and social factors. Qualitative studies are required to explore the patient journey pre and post hospital admission, which should focus on identifying facilitators and barriers to accessing treatment. Well-designed, controlled studies are needed to identify patient, social, and environmental factors associated with relapse to alcohol use after a diagnosis of ArLD. These data will enable us to adapt our support for patients to enhance engagement with services and improve long-term outcomes.

KEYWORDS

alcohol use disorder, alcohol-related liver disease, barriers, engagement, psychosocial factors

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BACKGROUND

Alcohol-related liver disease (ArLD) occurs in people who drink harmful amounts of alcohol (World Health Organization, 2007). The condition progresses from fatty liver (steatosis) to inflammation (steatohepatitis) and then scarring (cirrhosis), which is largely irreversible (European Association for the Study of the Liver, 2018). Alcoholic hepatitis is a severe complication that can occur at any stage of ArLD resulting in new-onset jaundice and coagulopathy and has a high risk of mortality of over 50% within 1 year (Louvet et al., 2017; Thursz, Richardson, et al., 2015). Outcome after diagnosis with ArLD is strongly influenced by alcohol consumption (Teli et al., 1995). In patients with steatosis, persistent alcohol use results in the development of cirrhosis in between 8% and 20% of cases (Lackner & Tiniakos, 2019). For those with established cirrhosis, patients who continue to drink have higher mortality, but abstinence, even after the development of advanced cirrhosis, can be beneficial in some (Borowsky et al., 1981; Pares et al., 1986). In patients who survive beyond 90 days after an episode of severe alcoholic hepatitis, there is a dose-dependent increase in the risk of mortality associated with alcohol use (Louvet et al., 2017). After diagnosis with ArLD or alcoholic hepatitis, reduction in harmful alcohol use is therefore the cornerstone of treatment to improve the long-term outcome of patients.

Several psychological and pharmacological treatments are effective in reducing alcohol-related harm in patients with ArLD although no single modality has shown superior efficacy (Khan et al., 2016; Mellinger & Winder, 2019). However, treatment of alcohol use disorder (AUD) is inconsistent across treatment settings and a large proportion of patients with ArLD do not receive appropriate therapy. In a large UK-randomized controlled trial in patients with severe alcoholic hepatitis, only 45% remained abstinent for greater than 90 days after diagnosis (Thursz, Forrest, et al., 2015). Fewer than 50% remained abstinent after 5 years from diagnosis with ArLD while 73% relapsed to alcohol use within 5 years after a diagnosis of alcoholic hepatitis (Gual et al., 2009; López-Pelayo et al., 2019).

Little is known about how social and psychological factors of patients with ArLD influence drinking behavior and access to or engagement with alcohol treatment services. Several tools exist to estimate the risk of relapse to harmful drinking such as the High-Risk Alcohol Relapse (HRAR) scale (Yates et al., 1993), which is based on prior drinking behavior. The Stanford Integrated Psychosocial Assessment for Transplantation also includes psychosocial factors to predict the risk of relapse post-liver transplantation (Maldonado et al., 2015). However, these tools have been developed using highly selected populations of liver transplant candidates that do not represent general patients with ArLD. These patients have fewer comorbidities and have already attained a period of abstinence from alcohol in order to be eligible for transplantation. Furthermore, it is more likely that they will have engaged with psychosocial support provided by addiction specialists based at liver transplant centres as part of the transplant assessment process.

It is apparent that many patients with ArLD or alcoholic hepatitis do not receive support or treatment for alcohol misuse and this is associated with poorer clinical outcomes. However, it is uncertain what factors are associated with ongoing alcohol consumption after a diagnosis of ArLD and what prevents or assists patient engagement with treatment.

Aim

The aim of this study was to conduct a review of the literature to identify factors associated with ongoing alcohol consumption in patients with ArLD including alcoholic hepatitis and barriers or facilitators to accessing or accepting treatment. Specifically, we searched for evidence of which patient characteristics and psychosocial factors were related to ArLD or alcoholic hepatitis and how this influenced engagement with healthcare services.

METHODS

A search of MEDLINE (the National Library of Medicine's bibliographic database of over 29 million biomedical journal citations) and EMBASE (a European-oriented database of biomedical journals and conference materials) was conducted in October 2020 using search strategies relating to ArLD or alcoholic hepatitis and the patient characteristics and psychosocial factors hypothesized to influence alcohol reduction, abstinence and/or engagement with healthcare services, and consisted of the following:

1. (TITLE ("alcoholic cirrhosis" OR "alcoholic hepatitis" OR "alcoholic liver disease" OR "alcohol related liver disease") AND TITLE-ABS-KEY (qualitative OR interview OR barriers OR coping OR acceptance OR feelings OR "patient experience" OR beliefs))
2. (TITLE ("alcoholic cirrhosis" OR "alcoholic hepatitis" OR "alcoholic liver disease" OR "alcohol related liver disease") AND TITLE-ABS-KEY (non-pharmacological OR psychological OR behavior* OR non-medical OR psychosocial OR motivational OR "social determinants" OR "social factors"))
3. (TITLE ("alcoholic cirrhosis" OR "alcoholic hepatitis" OR "alcoholic liver disease" OR "alcohol related liver disease") AND TITLE-ABS-KEY (mental-health OR wellbeing OR psychology* OR quality-of-life OR psychiatric))
4. (TITLE ("alcoholic cirrhosis" OR "alcoholic hepatitis" OR "alcoholic liver disease" OR "alcohol related liver disease") AND TITLE-ABS-KEY (barriers OR facilitators OR perceptions) AND TITLE-ABS-KEY (treatment))

The search was limited to studies published in English. Studies describing only patients assessed for liver transplantation or liver transplant recipients were excluded as these patients are not representative of general ArLD patients.

Titles and abstracts were reviewed by JH. Full texts were independently reviewed by JH and LC and were retained if they met the inclusion criteria of containing data relevant to either patient factors that drive ArLD or access to/acceptance of treatment. Relevant data were extracted and recorded in an electronic document and key themes were identified.

RESULTS

Initially, 1145 records were identified (Figure 1). Publications that did not meet inclusion criteria were discarded and 150 articles underwent a full-text screen, with 35 meeting inclusion criteria, detailed in Table S1.

Characteristics of patients with ArLD and alcoholic hepatitis

Patients with ArLD and alcoholic hepatitis have been well characterized in terms of age, gender, ethnicity, and socioeconomic status in randomized controlled trials or through interrogation of large datasets of routine data. In the UK, there is a rising number of patients with ArLD (Williams et al., 2014) who are middle-aged and predominantly male (Green et al., 2017).

Mental health and ArLD

Mental health symptoms and diagnoses are common in patients with ArLD. In a retrospective cohort study of 268 patients with ArLD, 12% of males and 43% of females had a formal psychiatric diagnosis, most commonly depression followed by anxiety (Taniai et al., 2012). Further, a prospective study of 73 patients with ArLD or alcoholic

hepatitis found that personality disorder was more common in patients with ArLD compared to the general population (18% vs. 8%; Yates et al., 1998).

In a random sample of 71 patients with ArLD and 71 controls with non-alcohol-related cirrhosis admitted to a tertiary hospital liver unit who underwent a structured psychiatric interview, 66% of ArLD patients (60% of males and 77% of females) had a previous or current mental health diagnosis compared with 32% of controls (Ewusi-mensah et al., 1984). Affective disorder, neurotic disorder, and antisocial personality were the commonest diagnoses. In a follow-up study of structured psychiatric interviews with 101 ArLD patients, 58% of them had psychopathology, which was positively correlated with the severity of alcohol dependence (Ewusi-Mensah et al., 1986). Using the primary care post-traumatic stress disorder (PTSD) questionnaire in 179 heavy drinkers with and without alcoholic hepatitis, PTSD prevalence was 34% (Samala et al., 2018) compared with a reported lifetime prevalence of 6.8% in the general population (Kessler et al., 2005). A diagnosis of PTSD was associated with higher alcohol use, but prevalence was similar between those with and without alcoholic hepatitis.

Although patients with alcoholic hepatitis have been studied in detail as part of several large RCTs, the opportunity to gather information on the prevalence of mental health needs and conditions has been missed. Mental health factors have only been reported in one recent Spanish cohort of 142 patients, of which 42% had psychiatric comorbidity (32% depression and anxiety and 10% personality disorder; Altamirano et al., 2017). This was not associated with mortality and did not predict the ability to maintain abstinence during a median follow-up of 55 months (Altamirano et al., 2017).

Social factors associated with ArLD

Occupational risk factors, social isolation, and poor social support have been linked to alcohol dependence (Collins, 2016). However, it is unknown whether this holds true for patients diagnosed with ArLD. Few studies have addressed this directly, but some have reported the social characteristics of ArLD patient cohorts. In a comparison of patients admitted to a London liver unit with a diagnosis of ArLD with non-alcohol-related cirrhosis controls, patients with ArLD were more likely to be older, not have a partner, have experienced the loss of their father in childhood, and have less frequent contact with family and friends (Farid et al., 1988, 1994). In addition, occupational risk factors were identified in ArLD patients but not in controls including shift work, availability of alcohol at the workplace, and flexible hours (Farid et al., 1994).

In a Japanese cohort of 21 patients who were followed up for 3 months after hospital admission, the only significant factor associated with readmission was the experience of personal loss such as the death of a relative or loss of a job within the previous year (Park et al., 2019). Patients who were readmitted also scored higher on the Profile of Mood States score in the anger-hostility and fatigue domains (Park et al., 2019).

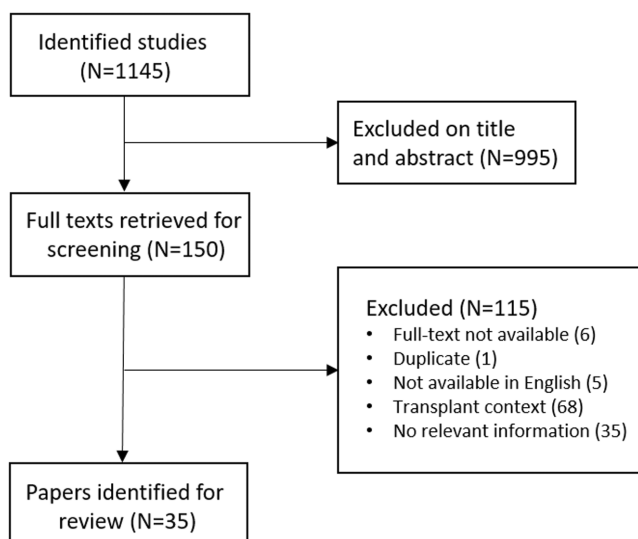


FIGURE 1 Flow chart of study selection process

In a cohort of 159 patients with ArLD, 19% were single, 26% lived alone and 19% were employed with 19% retired and 26% unemployed. None of these social factors were associated with depression or anxiety and were not related to an individual's illness perception (Lau-Walker et al., 2016).

Employment status varies considerably in reported studies with rates of unemployment ranging from 20% (Canha et al., 2017) in patients with ArLD to 70% in a French cohort with alcoholic hepatitis (Louvet et al., 2017) and 100% in 10 Swedish patients with ArLD (Mikkelsen et al., 2016). Employment status is likely to be influenced by local social and cultural factors, but there is a lack of comparative data to determine whether unemployment is higher in patients with ArLD than in matched controls.

Data from these studies suggest that psychosocial factors play an important part in an individual's decision to continue to drink alcohol after diagnosis with ArLD. Using detailed interviews with 24 individuals with ArLD, Blaxter and Cyster attempted to explore the reasons behind their drinking behavior (Blaxter & Cyster, 1984). One of the themes that were common to most patients was the social environment. Reduced alcohol consumption was easier to sustain in patients with stable partners or social groups or in those who had dependents or valued jobs. Patients reported the need to change their social activities to avoid exposure to peer pressure to drink (Blaxter & Cyster, 1984).

Barriers and facilitators of access to treatment

Our literature search did not identify any study that specifically investigated factors associated with accessing AUD treatment after a patient has been diagnosed with ArLD. Only a single study provided information on the setting of therapy (López-Pelayo et al., 2019). One study reported perceived barriers to AUD treatment in 22 patients with compensated or decompensated ArLD, the majority of whom were not actively drinking at the time (Mellinger et al., 2018). Stigma of alcohol misuse, anxiety around treatment in a group setting, and lack of anonymity were most frequently cited barriers. The importance of strong family and social relationships was recognized as an important motivator to change (Mellinger et al., 2018).

Qualitative studies involving in-depth patient interviews identify some common themes that influence a patient's drinking behavior. Firstly, clear communication with the patient is paramount. Patients who had a poor understanding of their underlying condition were less likely to reduce alcohol consumption (Blaxter & Cyster, 1984; Presky et al., 2018). Furthermore, good communication can reduce patients' misconceptions about AUD treatment such as that treatment is futile or that it is not required if they are currently abstinent (Mellinger et al., 2018). Conversations between medical staff and patients while the patient is unwell in hospital can be poorly recalled and patients are often provided with little written information on discharge (Blaxter & Cyster, 1984). A poor understanding of their condition is also associated with lower confidence in self-management (Lau-Walker et al., 2016).

Secondly, a lack of symptoms can reinforce the belief that the patient does not require treatment (Blaxter & Cyster, 1984; Mellinger et al., 2018; Presky et al., 2018). This can often be the case as chronic liver disease is usually asymptomatic until advanced stages. Those with more physical symptoms or a perception that their condition was progressing were more likely to maintain abstinence (Blaxter & Cyster, 1984). However, patients with a higher number and frequency of illness-related symptoms were less confident in managing their condition (Lau-Walker et al., 2016).

Thirdly, patients who perceived a lack of control over their condition were less likely to adhere to treatment or remain abstinent (Lau-Walker et al., 2016; Presky et al., 2018). Lack of control has a negative impact on health behavior change and can undermine an individual's confidence in self-management (Lau-Walker et al., 2016; Presky et al., 2018).

A retrospective cohort study of 120 patients with alcoholic hepatitis investigated baseline factors that predicted retention in an alcohol treatment programme run by an addiction specialist (López-Pelayo et al., 2019). Long-term retention was more likely in those with psychiatric comorbidities, severe alcohol dependence, and advanced cirrhosis. Relapse to drinking was predicted by an HRAR score greater than three and treatment undertaken at different centres to the index presentation (López-Pelayo et al., 2019). This suggests that familiarity with the location or treating team may enhance patient engagement in treatment. The importance of a strong patient-clinician relationship was also identified as a facilitator of alcohol treatment in a second study (Mellinger et al., 2018).

DISCUSSION

It is recognized that psychosocial factors strongly influence an individual's behavior related to alcohol use, but this review found that most clinical trials or cohort studies that have been conducted in patients with ArLD do not collect or report such data. There is instead, a focus on liver-related outcomes and overall mortality (Buzzetti et al., 2017). A number of small observational studies described the influence of social support and occupation on alcohol use, which was explored in-depth in a qualitative study. This study found that being a valued member of society (having a social network, dependents, and a valued job) enabled a sustained reduction in alcohol use in patients with ArLD (Lau-Walker et al., 2016).

The interaction between chronic alcohol consumption and mental health is well established (McHugh & Weiss, 2019). Dual diagnosis of AUD and a psychiatric disorder is associated with greater severity and worse prognosis than either diagnosis alone (Greenfield et al., 1998). Alcohol is also frequently used by patients with mental health conditions to self-medicate (Crum et al., 2013). Therefore, it is not surprising that patients with ArLD have a high incidence of mental health symptoms and diagnoses.

Recommendations for psychological and pharmacological therapy have been published for patients with ArLD (Addolorato et al., 2016; Mellinger & Winder, 2019), which recognize difficulties

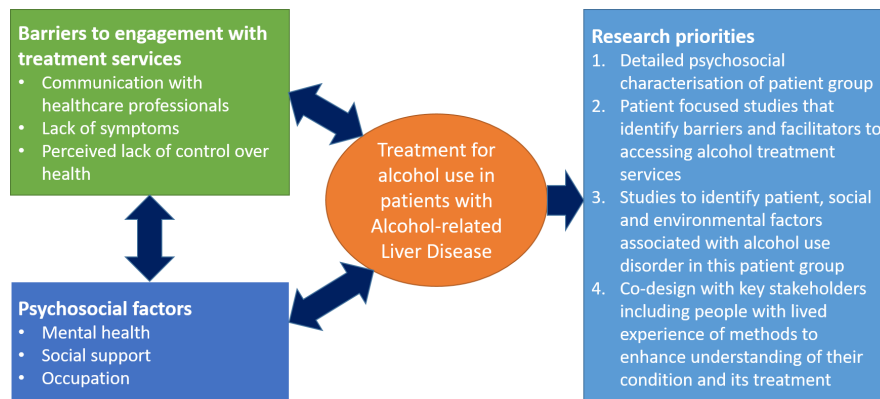


FIGURE 2 Summary of key findings and research priorities identified

in engaging patients and emphasize the importance of a multidisciplinary team approach with consideration of the most appropriate location for treatment (Addolorato et al., 2016). Our review identified several common themes explaining the challenges patients with ArLD face when engaging with alcohol services. Patients with a poor understanding of their condition, due to ineffective communication with healthcare professionals, together with a lack of physical symptoms are more likely to hold a belief that they do not require support or treatment for alcohol use. While patients who perceived a lack of control over their health had more passive behaviors and reduced confidence in self-management. These factors must be addressed when designing alcohol services.

Evidence gaps

This literature review demonstrates that there are limited data in patients with ArLD regarding factors associated with alcohol abstinence, adherence to treatment, and barriers or facilitators to treatment. There is evidence that the same psychosocial issues found in patients with AUD are also present in patients with ArLD. Mental health diagnoses of depression, anxiety, and PTSD are common in these patients. Social support and occupational factors have also been documented to be important in relation to alcohol use. The challenges of co-occurring conditions interacting with multiple and complex psychosocial factors may affect individuals' engagement with traditionally delivered services that require proactive engagement by patients.

Furthermore, there are few studies from a patient perspective. Most studies report only basic demographic information and focus on liver-related outcomes. Only one recent alcoholic hepatitis study reports on the effect of mental health diagnoses on long-term abstinence (Altamirano et al., 2017). There are no studies describing the patient journey prior to and after hospital admission, which is important both to help identify opportunities for intervention and to design services that are acceptable and accessible to patients. This review did not specifically evaluate the impact of alcohol service design on patient engagement with treatment, but

it is clear from the literature that there are challenges in maintaining continuity between secondary and community care settings as evidenced by low rates of follow-up with community alcohol services after hospital discharge (Thursz, Forrest, et al., 2015). A recent expert consensus paper recommends the commencement of alcohol rehabilitation in hospital with continuation in the community but does not provide a framework for achieving this (Thursz et al., 2019). An improved understanding of how psychosocial factors influence an individual's behavior related to both alcohol use and engagement in treatment is needed to be able to develop robust alcohol treatment programs.

There is limited evidence from a handful of qualitative studies to suggest that clarity of doctor-patient communication and improved understanding of their condition can enhance future health behavior. Providing patients with strategies to take control of their health may also be beneficial although methods to do this have not been investigated in the context of ArLD.

Recommendations for future study (Figure 2)

1. Clinical studies of patient cohorts with ArLD should include detailed psychosocial assessments to capture information on mental health and social factors. As a minimum, this should document any pre-existing mental health diagnosis and details on occupation, living arrangements, and dependents.
2. Qualitative studies are required to explore the patient journey before, during, and after hospital admission, which should focus on identifying facilitators and barriers to accessing and engaging with treatment including where alcohol services are based and how they are designed and delivered.
3. Studies are needed to identify patient, social, and environmental factors associated with relapse to alcohol use after a diagnosis of ArLD. These should include a comparator group of patients with AUD without ArLD.
4. Standardized methods to enhance patient understanding about their condition and the consequences of sustained alcohol use or abstinence should be trialed in patients with ArLD and their effect

on continued alcohol consumption investigated. Such methods should be co-designed by relevant stakeholders including those who have a lived experience of ArLD.

CONCLUSION

Reducing alcohol use in patients with ArLD is the pivotal strategy to reduce long-term alcohol-related harm. Methods to support patients in alcohol reduction and cessation are available but need to be redesigned to promote access and engagement. We now need to understand what changes are required in reconfiguring alcohol services by taking into account system- and patient-oriented factors that are barriers to accessing help and treatment (Figure 2). In doing so, we can support patients with ArLD to enhance their engagement and improve their long-term outcomes.

CONFLICT OF INTEREST

None of the authors have any conflict of interest to declare.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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