The impact of liver disease on patients’ quality of life: a mixed methods systematic review protocol

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ABSTRACT

Objective: The objective of this systematic review is to explore the impact of liver disease on patients’ quality of life in an attempt to develop effective evidence-based recommendations and strategies useful for clinical practice and health care professionals.

Introduction: Liver diseases are common worldwide and a major cause of illness and death due to health problems and serious complications, which not only cause hospitalization and death, but also emotional distress, depression, and impaired quality of life.

Inclusion criteria: This review will consider qualitative and quantitative studies on patients with liver disease of different severity and type. The qualitative component of this review will consider all studies that describe patients’ lived experience and perception of having liver disease. The quantitative component will include studies that explore the quality of life in patients with liver disease.

Methods: CINAHL (EBSCO), Embase (Ovid), MEDLINE (Ovid), PsycINFO (Ovid), Scopus (Elsevier), and Web of Science (Ovid) will be searched for articles published in Danish and English without any restriction in terms of year of publication. Articles describing both qualitative and quantitative studies will be screened for inclusion, critically appraised for methodological quality, and have data extracted using JBI instruments for mixed methods systematic reviews. A convergent integrated approach to synthesis and integration will be used.

Systematic review registration number: PROSPERO with ID number (CRD42020173501)

Keywords liver disease; mixed method; patient experience; quality of life; systematic review

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Introduction

Liver diseases, including alcoholic liver disease, autoimmune liver disease, hepatitis B and C virus, nonalcoholic fatty liver disease, and associated cirrhosis and hepatocellular carcinoma are very common worldwide and a major cause of illness and death.\(^1\,^2\)

Regardless of the type of liver disease, the disease is likely to progress in the same way. In the early stage, liver disease is characterized by inflammation of the liver.\(^2\,^3\) Chronic liver inflammation leads to unrelenting fibrosis deposition with formation of scars that progressively disrupt the normal liver architecture and function. Cirrhosis is the final pathway for liver disease. It is an advanced stage of fibrosis, defined as the histological development of regeneration nodules surrounded by fibrous tissue, which results in portal hypertension and hepatic dysfunction.\(^2\,^3\) Unless liver transplantation is performed, liver diseases may cause serious health problems, hospitalization, and death due to its poor long-term clinical outcome.\(^3\,^4\)

The prevalence of liver disease is difficult to assess, because it may be asymptomatic at first so the disease is often undiagnosed. Available data suggest that 0.25% of the European population and 0.27% of the American population is affected by liver disease.\(^5\,^6\) However, recent data suggest a dramatic increase in liver disease over recent decades as opposed to the trend of declining rates for most chronic diseases.\(^1\,^7\)

Patients’ experience of liver disease and their quality of life have become essential components...
when exploring the impact of illness. The World Health Organization defines quality of life as “individuals’ perception of their position in life in the context of the culture and value systems in which they live and in relation to their concerns, expectations, goals, and standards. It is a broad ranging concept affected in a complex way by the individual’s physical health, psychological state, level of independence, personal beliefs, social relationships, and their relationship to salient features of their environment." In light of the increased numbers of this patient group, it is important that health care professionals understand the experience and perception of patients with liver disease in relation to their disease beyond their medical care and treatment in order to ensure a satisfying quality of life.

Studies have found that patients with liver disease experience a significant burden of illness leading to depression, distressing emotions, and worse quality of life compared to healthy controls. Having liver disease may result in mental and physical complications and symptoms such as anxiety, ascites, change of body image, depression, esophageal varices, hepatic encephalopathy, impaired mobility, irregular sleep patterns, and muscle cramps. In addition, the liver disease can affect the person’s ability to drive and to work, which may lead to a negative impact on their finances and socioeconomic status. These mental, physical, and social challenges impair the quality of life of the patients and cause hospitalization and readmissions. Both qualitative and quantitative studies have addressed the impact of liver disease on patients’ quality of life. However, there has been no systematic review undertaken integrating both qualitative and quantitative studies, to explore the impact of liver disease on patients’ quality of life. Therefore, it is anticipated that this systematic review will provide a more detailed understanding and contribute new knowledge. The evidence generated from this mixed method systematic review will increase health care professionals’ knowledge and assist in the provision of information to develop effective evidence-based recommendations and strategies useful for clinical practice and health care professionals.

Before commencing the review, the researchers reviewed Cochrane Library, JBI Evidence Synthesis, and PubMed to ensure that there is no current activity pertaining to the review objectives.

**Review question**

How is patients’ quality of life affected by having liver disease?

**Inclusion criteria**

**Participants**

This review will consider studies that include patients who have liver disease. Studies will be considered regardless of liver disease severity and type, patients’ age, ethnicity, or gender. Studies on the experience and quality of life of relatives or health care professionals will not be included in the review.

**Phenomena of interest**

The qualitative component of this review will consider, but is not limited to, studies that explore patients’ emotional, physical, psychosocial, spiritual, and financial experiences and perceptions of having a liver disease.

The quantitative component of this review will consider studies whose primary aim is to explore quality of life in patients with liver disease using either disease-specific or generic questionnaires that are generally accepted as reliable and valid to measure health-related quality of life. The questionnaires may measure quality of life, but are not limited to the cognitive, emotional, physical domains, role, social function, and general health. Studies comparing patients with liver disease with healthy control groups or a sample of the general population will be included; however, studies comparing patients with different liver diseases or patients with liver disease with other patient groups will be excluded. In addition, studies that explore patients’ changes in quality of life over time in connection with different, clinical interventions or in studies testing new medicines will not be included in the review. Finally, studies exploring the experience of awaiting or receiving a liver transplantation and the impact on quality of life will not be included in the review.

**Context**

Clinical settings may be varied and could include all hospitals, community settings, primary care, and any geographic location.

**Type of studies**

This review will consider both mixed-method, qualitative, and quantitative studies. Mixed method
studies will only be considered if data from the qualitative and quantitative component can be clearly extracted. Qualitative studies will be included regardless of design and method. Quantitative studies will include observational analytic/descriptive studies (case-control studies, cross-sectional studies, prospective and retrospective cohort studies).

**Methods**

The proposed mixed method systematic review will be conducted in accordance with JBI methodology for convergent integrated mixed methods systematic reviews\(^2^7\) and the Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) guidelines.\(^2^8\) The review protocol has been registered in PROSPERO (CRD42020173501).

**Search strategy**

The search strategy will be developed with a hospital librarian. The search strategy aims to identify both published and unpublished studies. A three-step search strategy will be utilized for each component of this review. First, an initial limited search of CINAHL (EBSCO) and MEDLINE (Ovid) will be undertaken followed by an analysis of the words contained in the relevant article title and abstract, and of the index terms used to describe the article. Second, another search using all identified keywords and index terms will be undertaken across all included databases. Third, the reference list of all articles selected for critical appraisal and possible inclusion will be obtained and assessed for eligibility by the previous two reviewers. Reasons for excluding any full-text articles will be recorded and reported in the review. At any step of the article-selection phase, disagreement between reviewers about the inclusion or exclusion of studies will be resolved through discussion. The phases and result of the study selection will be reported in the final review and presented in a PRISMA flow diagram.\(^2^8\)

**Assessment of methodological quality**

Two independent reviewers will assess the methodological quality of the studies described in the selected full-text articles. Qualitative (and qualitative components of mixed method studies) and quantitative studies (and quantitative components of mixed method studies) will be critically appraised using the standardized critical appraisal instrument from JBI SUMARI.\(^2^7\) All studies will be included, regardless of methodological quality. The result of critical appraisal will be reported in narrative form and in a table. In addition, a discussion on the methodological quality of the studies and the possible impact will be reported in the review. Disagreement between the reviewers about the quality of the studies will be resolved through discussion.

**Data extraction**

Qualitative and quantitative data will be extracted from the studies described in the full-text articles included in the review using the standardized JBI
data extraction instrument JBI SUMARI.\textsuperscript{27} The data extracted will include specific details about the study method, population, phenomena of interest, context, and outcome of relevance to the review question. Specifically, qualitative data will comprise of themes or subthemes with corresponding illustrations, and will be assigned a level of credibility. In addition, quantitative data will comprise data-based outcomes of descriptive and/or inferential statistical tests. Two independent reviewers will extract data and any disagreement will be resolved through discussion.

**Data transformation, synthesis, and integration**

Following data extraction, quantitative data will be transformed into qualitized data to facilitate the integration with data extracted from qualitative studies (and qualitative components of mixed methods studies). This will involve quantitative data being transformed into textual descriptions or narrative interpretation of the quantitative findings to respond directly to the review question.

This review will follow a convergent integrated approach according to JBI methodology for mixed methods systematic reviews using JBI SUMARI.\textsuperscript{27} This will involve assembling the qualitized data with the qualitative data. Assembled data will be categorized and pooled together based on similarity in meaning to produce a set of integrated findings in the form of line action statements to develop effective evidence-based recommendations and strategies useful for clinical practice and health care professionals’ recommendations.

**Funding**

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**References**

21. Younossi ZM, Guyatt G, Kiwi M, Boparai N, King D. Development of a disease specific questionnaire to measure
## Appendix I: Search strategy

### MEDLINE (Ovid)

<table>
<thead>
<tr>
<th>Search ID Terms</th>
<th>Search terms</th>
</tr>
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<tr>
<td>S1</td>
<td>(Quality of life) OR (Mesh “Quality of life”)</td>
</tr>
<tr>
<td>S2</td>
<td>(Experience) OR (“Lived experience”) OR (“Patient experience”)</td>
</tr>
<tr>
<td>S3</td>
<td>(Perception) OR (Mesh “Perception”)</td>
</tr>
<tr>
<td>S4</td>
<td>(Impact)</td>
</tr>
<tr>
<td>S5</td>
<td>(Attitude) OR (Mesh “Attitude”)</td>
</tr>
<tr>
<td>S6</td>
<td>(Behavior) OR (Mesh “Behavior”)</td>
</tr>
<tr>
<td>S7</td>
<td>(Qualitative research) OR (Mesh “Qualitative research”)</td>
</tr>
<tr>
<td>S8</td>
<td>(Qualitative study) OR (Mesh “Qualitative study”)</td>
</tr>
<tr>
<td>S9</td>
<td>S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8</td>
</tr>
<tr>
<td>S10</td>
<td>(Liver disease) OR (Mesh “Liver disease”)</td>
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<td>S11</td>
<td>(Chronic liver disease)</td>
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<td>S12</td>
<td>(Cirrhosis) OR (Liver cirrhosis) OR (Mesh “Liver cirrhosis”)</td>
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<td>(Fibrosis) OR (“Liver fibrosis”)</td>
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<tr>
<td>S14</td>
<td>(“End-stage liver disease”) OR (Mesh “End-stage liver disease”)</td>
</tr>
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<td>S15</td>
<td>S10 OR S11 OR S12 OR S13 OR S14</td>
</tr>
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<td>S16</td>
<td>S9 AND S15</td>
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</table>

Search retrieved 1783 hits  
Conducted on March 20, 2020

**Legend**

- **Mesh** – Medical Subject Heading / MeSH term  
- () – Keywords will be searched in this order: MeSh, Journals, Authors  
- **Limits**  
  - Danish or English language