ISSN 1948-5182 (online)

World Journal of *Hepatology*

World J Hepatol 2021 November 27; 13(11): 1459-1815

Published by Baishideng Publishing Group Inc

World Journal of Hepatology

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INDEXING/ABSTRACTING

The *WJH* is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), Scopus, China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (CSTJ), and Superstar Journals Database. The 2021 edition of Journal Citation Reports® cites the 2020 Journal Citation Indicator (JCI) for *WJH* as 0.61. The *WJH*'s CiteScore for 2020 is 5.6 and Scopus CiteScore rank 2020: Hepatology is 24/62.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Xu Guo*; **Production Department Director:** *Xiang Li*; **Editorial Office Director:** *Xiang Li*.

NAME OF JOURNAL
World Journal of Hepatology

ISSN
ISSN 1948-5182 (online)

LAUNCH DATE
October 31, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Nikolaos Pyrsopoulos, Ke-Qin Hu, Koo Jeong Kang

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-5182/editorialboard.htm

PUBLICATION DATE
November 27, 2021

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World J Hepatol 2021 November 27; 13(11): 1642-1652

DOI: 10.4254/wjh.v13.i11.1642

ISSN 1948-5182 (online)

MINIREVIEWS

Health-related quality of life in autoimmune hepatitis

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Author contributions: Gevers TJ had the original idea and supervised the study; Gevers TJ and Snijders RJ performed the research; Snijders RJ wrote the manuscript; Milkiewicz P and Schramm C contributed equally to this work; All authors critically reviewed the manuscript and approved the final version of the manuscript.

Conflict-of-interest statement: All authors report no potential conflicts that are relevant to the manuscript.

Country/Territory of origin: Netherlands

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

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Abstract

Autoimmune hepatitis (AIH) is a severe chronic autoimmune disease and has a significant impact on the patient's quality of life, in particular regarding psychological problems such as anxiety and depression. Consistent evidence on which patient-related, disease-related or physician-related factors cause health-related quality of life (HRQoL) impairment in patients with AIH is lacking. Current studies on HRQoL in AIH are mainly single-centered, comprising small numbers of patients, and difficult to compare because of the use of different questionnaires, patient populations, and cutoff values. Literature in the pediatric field is sparse, but suggests that children/adolescents with AIH have a lower HRQoL. Knowledge of HRQoL and cohesive factors in AIH are important to improve healthcare for AIH patients, for example by developing an AIH-specific chronic healthcare model. By recognizing the importance of quality of life beyond the concept of biochemical and histological remission, clinicians allow us to seek enhancements and possible interventions in the management of AIH, aiming at

Received: March 25, 2021
Peer-review started: March 25, 2021
First decision: June 4, 2021
Revised: June 15, 2021
Accepted: August 16, 2021
Article in press: August 16, 2021
Published online: November 27, 2021

P-Reviewer: Shahini E
S-Editor: Gao CC
L-Editor: Filipodia
P-Editor: Li JH

improved health.

Key Words: Autoimmune hepatitis; Quality of life; Depression; Anxiety; Corticosteroids

Core Tip: Autoimmune hepatitis (AIH) is a severe chronic autoimmune disease and has a significant impact on the patient's quality of life, in particular regarding psychological problems such as anxiety and depression. The health-related quality of life (HRQoL) of patients with AIH can be affected by various patient-related, disease-related, and physician-related factors. In this review we summarized several specific factors that are liable to influence HRQoL in AIH. By recognizing the importance of quality of life beyond the concept of biochemical and histological remission, clinicians allow us to seek enhancements and possible interventions in the management of AIH.

Citation: Snijders RJ, Milkiewicz P, Schramm C, Gevers TJ. Health-related quality of life in autoimmune hepatitis. *World J Hepatol* 2021; 13(11): 1642-1652
URL: https://www.wjgnet.com/1948-5182/full/v13/i11/1642.htm
DOI: https://dx.doi.org/10.4254/wjh.v13.i11.1642

INTRODUCTION

Autoimmune hepatitis (AIH) is a severe chronic autoimmune disease that occurs mainly in women and affects health-related quality of life (HRQoL) worldwide. The diagnosis of AIH is based on the presence of autoantibodies, typical features on liver histology, and increased immunoglobulin G (IgG) levels[1]. The presentation of AIH is variable, ranging from mild and asymptomatic disease to fulminant hepatic failure. Nonspecific symptoms at presentation are fatigue, anorexia, jaundice, and abdominal pain, whereas others are asymptomatic at disease onset[1]. The majority of patients need lifelong treatment to prevent disease progression to cirrhosis and/or decompensation[2]. Current treatment strategies in AIH include administering corticosteroids (mainly prednisolone) and a long-term corticosteroid-saving regime, including azathioprine (AZA) as first-line treatment[3,4]. Second-line immunosuppressants include mycophenolate mofetil (MMF), calcineurin inhibitors (CNIs), and mercaptopurine and have proven to be effective in mainly uncontrolled studies[5].

The main goal of AIH treatment is to achieve complete biochemical and histological remission without the occurrence of side effects. Alanine aminotransferase, aspartate aminotransferase and IgG serum levels are used as parameters to monitor biochemical response, and current guidelines advocate pursuit of normalization of those parameters as the aim of treatment. As a result, treatment failure, defined as absence of normalization of transaminases, triggers clinical actions such as increase of drug dose or change in drug class. A sole focus on biochemical response is insufficient when managing AIH. From a patient perspective, other aspects that affect HRQoL, including but not limited to side effects, psychological health, and implications of the disease, are just as important.

One of the main objectives relating to AIH according to the International Autoimmune Hepatitis Group (IAIHG), is better assessment of HRQoL in patients. However, literature or guidelines on that topic in AIH are scarce and inconsistent. An update on current literature on HRQoL in AIH, is warranted to reveal the most important research gaps[6]. Understanding which potentially treatable factors are associated with reduced quality of life in patients with AIH is essential for development of interventions targeting well-being. The focus of this paper is to review the current knowledge of HRQoL and associated factors in AIH, to comment on the current status, and to identify future perspectives that may influence and benefit disease management of adult patients with AIH.

METHODOLOGY

We searched the titles, abstracts, and MeSH terms of articles indexed in PubMed using the keywords "autoimmune hepatitis," "AIH," "health-related quality of life," and "quality of life." The search was limited to articles published before January 27, 2021. We included articles based on the following criteria: (1) Full-text articles published in peer-reviewed journals; (2) English or Dutch articles; (3) Publication dates within the last 20 years at the time of the search; and (4) Either adult or pediatric AIH. The search retrieved 116 publications; 39 were evaluated in full-text after screening the titles and abstracts (Figure 1). We also checked the reference lists of the included articles to identify other articles. For the purpose of this review, we primarily focused on articles addressing the role of HRQoL in AIH.

HRQOL IN ADULT PATIENTS WITH AIH

Several studies have reported reduced general or liver-specific HRQoL in AIH patients (Tables 1 and 2)[7-15]. The first study published was conducted in the Netherlands and showed a reduced quality of life in 141 patients with AIH compared with healthy controls, using three instruments, the SF-36 for generic HRQoL, the Multidimensional Fatigue Index-20, and the Liver Disease Symptom Index 2.0, which is a liver-specific questionnaire addressing nine topics. In particular, patients had lower scores in subscales measuring physical problems or general health. Patients with AIH mentioned fatigue more often than healthy controls did[13]. A landmark study performed in Germany compared 102 AIH patients to the German general population and to published data of patients with arthritis using the SF-12[12]. They reported lower mental well-being in patients with AIH compared with both groups, but the physical component score (PCS) was unaffected[12]. A Polish single-center study showed that patients with AIH (n = 140) scored significantly worse in all subscales of the SF-36, except for one measuring the impact of emotional problems on work and daily activities[15]. The majority of the AIH patients in that cohort had cirrhosis (55%), and as in the previously mentioned study, that did not have a significant effect on well-being. A recent Italian multicenter study of chronic liver disease reported that of a total of seven different chronic liver diseases without cirrhosis, patients with AIH had a lower quality of life measured with the EQ-5D VAS score, and experienced difficulties in the self-care domain, even after adjusting for multiple possible confounders, including age, sex, education, and professional status[10]. That was confirmed in a Cuban study in which AIH patients had lower quality of life scores than hepatitis B patients using the disease-specific Chronic Liver Disease Questionnaire (CLDQ)[7]. Only one meta-analysis was performed, including three studies that evaluated HRQoL measured with the SF-36. The analysis confirmed reduction of the PCS and mild reduction of the mental component score in patients with AIH. However, they included only older studies and compared all AIH patients (including Dutch and German patients) to the United States general population norm [16]. Finally, the largest study conducted so far involved multiple health centers in the United Kingdom and confirmed previous results by finding that the HRQoL of patients with AIH (n = 990) was worse than it was in the general population, adjusted for age and gender and using the EQ-5D-5L[14]. Although these studies consistently report a lower HRQoL in AIH, albeit in varying domains, it remains difficult to compare the studies because of the use of different questionnaires (EQ-5D-5L *vs* SF-12 or SF-36 *vs* CLDQ), cutoff values, methodology, and patient populations. Moreover, most studies were conducted at single centers and included small numbers of participants, thereby introducing bias based on the heterogenicity in study populations (*e.g.*, remission status and demographic differences).

HRQOL IN PEDIATRIC PATIENTS WITH AIH

A lower HRQoL was also found in children and adolescents with AIH, although literature in the pediatric field is sparse[17-19]. A study performed in Portugal compared 43 children with AIH to 62 healthy children using the Pediatric Quality of Life Inventory 4.0 (PedsQL 4.0)[17]. They found that especially children with associated comorbidities (*e.g.*, inflammatory bowel disease, hemolytic anemia, and hypothyroidism) had a lower quality of life. That was confirmed in a Brazilian cohort using the same questionnaire[18]. Interestingly, the evaluation of HRQoL in the

Table 1 Overview of the studies assessing aspects of health-related quality of life in autoimmune hepatitis

Ref.	Country	Population (*n*)	Biochemical remission (%)	Cirrhosis (%)	Questionnaire	Factors/results
van der Plas *et al* [13], 2007	The Netherlands	AIH (142), other liver diseases (776)	-	-	SF-36, MFI-20, LDSI	HRQoL impairment; Association with: Fatigue
Afendy *et al*[8], 2009	United States, Italy	AIH (13), other chronic liver diseases (1090)	-	84.6[1]	SF-36	HRQoL impairment; Negative correlation: Age (every scale), female gender (primary predictor of mental health), cirrhosis (every scale, primary predictor of physical health)
Schramm *et al* [12], 2014	Germany	AIH (103)	77	27	SF-12, PHQ-9, GAD-7	HRQoL impairment (total mental score/mental well-being); Association with: depression and anxiety (positive correlation with female gender, corticosteroid use, and concerns about progression of the liver disease)
Takahashi *et al* [11], 2018	Japan	AIH (265), chronic hepatitis C (88)	-	10.6	CLDQ, SF-36	HRQoL impairment; Negative correlation: Age, cirrhosis, comorbid diseases, corticosteroid use (worry domain), disease duration, AST; Positive correlation: platelet count
Wong *et al*[14], 2018	United Kingdom	AIH (990)	56	33	EQ-5D-5L, FIS, CFQ, HADS	HRQoL impairment; Positive correlation: Biochemical remission; Negative correlation: overlap syndromes, corticosteroid use, and calcineurin inhibitor use
Janik *et al*[15], 2019	Poland	AIH (140)	-	55	SF-36, MFIS, PHQ-9, STAI	HRQoL impairment (every scale, except role emotional[2]); Negative correlation: Female gender, depression, trend toward better HRQoL (physical health) with budesonide *vs* prednisone; Association with: Anxiety, depression, and fatigue
Dirks *et al*[9], 2019	Germany	AIH (27), AIH/PBC (8), other liver diseases (97)	-	0	SF-36, FIS, HADS	HRQoL impairment; Association with: Anxiety, depression, and fatigue
Castellanos-Fernández *et al*[7], 2021	Cuba	AIH (22), overlap syndrome of AIH and PBC (7), PBC (14), other liver diseases (500)	-	43.9[3]	FACIT-F, WPAI:SHP, CLDQ	HRQoL impairment; Positive correlation: Male gender, exercising > 90 min/wk; Negative correlation: Fatigue, abdominal pain, anxiety, depression, and extrahepatic comorbidity (diabetes mellitus type 2, sleep apnea)
Cortesi *et al*[10], 2020	Italy	AIH (51), other chronic liver diseases (2911)	-	0	EQ-5D-3L	HRQoL impairment in AIH

[1]Eight patients with Child-Pugh class A and three patients with Child-Pugh class C.
[2]Scale measures the impact of emotional problems on work and daily activities.
[3]Cirrhosis in patients with autoimmune liver diseases (n = 43). AIH: Autoimmune hepatitis; HRQoL: Health-related quality of life; PBC: Primary biliary cholangitis; AST: Aspartate aminotransferase; CFQ: Cognitive failure questionnaire; CLDQ: Chronic liver disease questionnaire; ECR: Experiences in close relationship scale; EQ-5D-5L/3L: European quality of life 5-dimension 5-level/3-level; FACIT-F: Functional assessment of chronic illness therapy-fatigue; FIS: Fatigue impact scale; GAD-7: Generalized anxiety disorder screener; HADS: Hospital anxiety depression scale; LDSI: Liver disease symptom index 2.0; MFI-20: Multidimensional fatigue index-20; PHQ-9: Patient health questionnaire; SF-12: Short-form 12; SF-36: Short-form 36; STAI: State-trait anxiety inventory; WPAI:SHP: Work productivity and activity-specific health problem.

parents differed from the children's self-reports[18]. Only the physical and total scores were significantly lower in patients with AIH based on the parental reports, whereas in the children's reports the emotional, school, physical, and total scores were significantly lower.

Table 2 Overview of the questionnaires assessing aspects of health-related quality of life in autoimmune hepatitis

Questionnaire	Main function	Domains	Items, total score
CFQ[41]	Cognition	Memory, attention, concentration, forgetfulness, word-finding abilities, and confusion	25 items scored 0-4, total score 0-100
CLDQ[42]	Generic HRQoL	Abdominal symptoms, fatigue, systemic symptoms, activity, emotions, and worry	29 items scored 1-7, total score 29-203
ECR[43]	Relationship styles	ECR-anxiety, and ECR-avoidance	12 items scored 1-7, each scale total score 7-42
EQ-5D-5L/EQ-5D-3L/EQ-VAS [44]	Generic HRQoL, EQ-VAS: participants' self-rated health on a visual analog scale	Mobility, self-care, usual activities, pain/discomfort, and anxiety/depression	EQ-5D: 5 items scored 1-5, total score 5-25; EQ-VAS: total score 0-100
FACIT-F[45]	Fatigue	Physical well-being, social well-being, emotional well-being, functional well-being, and a fatigue-specific domain	40 items scored 0-4, total score 0-160
FIS[46]	Fatigue	Cognitive functioning, physical functioning, and psychosocial functioning	40 items scored 0-4, total score 0-160
GAD-7[47]	Anxiety	-	7 items scored 0-3, total score 0-21
HADS[48]	Anxiety, depression	Anxiety, and depression	14 items scored 0-3, total score 0-42
LDSI[49]	Liver disease symptoms	Itch, joint pain, abdominal pain, daytime sleepiness, worry about family situation, decreased appetite, depression, fear of complications, and jaundice (+ symptom hinderance)	18 items scored 1-5, total score 18-90
MFI-20[50]	Fatigue	General fatigue, physical fatigue, reduction in activity, reduction in motivation, and mental fatigue	20 items scored 1-5, each domain total score 4-20
MFIS[46,51]	Fatigue	Physical, cognitive, and psychosocial functioning	21 items scored 0-4, total score 0-84
PHQ-9[52]	Depression	Anhedonia, feeling down, sleep, feeling tired, appetite, feeling bad about self, concentration, activity, and suicidality	9 items scored 0-3, total score 0-27
SF-12[53]	Generic HRQoL	Physical functioning, role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health	12 items scored 1-5, total score 0-100
SF-36[54]	Generic HRQoL	General health, physical and social functioning, bodily pain, role-physical, mental health, role-emotional, and vitality	36 items, total score 0-100
STAI[55]	Anxiety	State anxiety, and trait anxiety	40 items scored 1-4, total score 0-80
WPAI:SHP[56]	Impairment in daily activities and in work	Work productivity impairment, and activity impairment	6 items scored 0-10, total score -

Included in the table are the questionnaires that were employed in the reviewed studies. CFQ: Cognitive Failure Questionnaire; CLDQ: Chronic Liver Disease Questionnaire; ECR: Experiences in Close Relationship Scale; EQ-5D-5L/EQ-5D-3L/EQ-VAS: European Quality of life 5-Dimension 5-Level/3-Level/EQ-visual analog scale; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; FIS: Fatigue Impact Scale; GAD-7: Generalized Anxiety Disorder Screener; HADS: Hospital Anxiety Depression Scale; LDSI: Liver Disease Symptom Index 2.0); MFI-20: Multidimensional Fatigue Index-20; MFIS: Modified Fatigue Impact Scale); PHQ-9: Patient Health Questionnaire; SF-12: Short-form 12; SF-36: Short-form 36; STAI: State-Trait Anxiety Inventory; WPAI:SHP: Work Productivity and Activity-Specific Health Problem).

DETERMINANTS OF HRQOL IN AIH

The HRQoL of patients with chronic diseases can be affected by various patient-related, disease-related, and physician-related factors. We have summarized the patient-, disease- and physician-related factors that are liable to influence HRQoL in AIH in Figure 2.

Patient-related factors

Patients with AIH are more often diagnosed with symptoms of depression and anxiety compared with the general population or healthy controls[7,9,10,12,15]. Studies by Schramm and Janik *et al*[15] showed a significantly higher percentage of depression

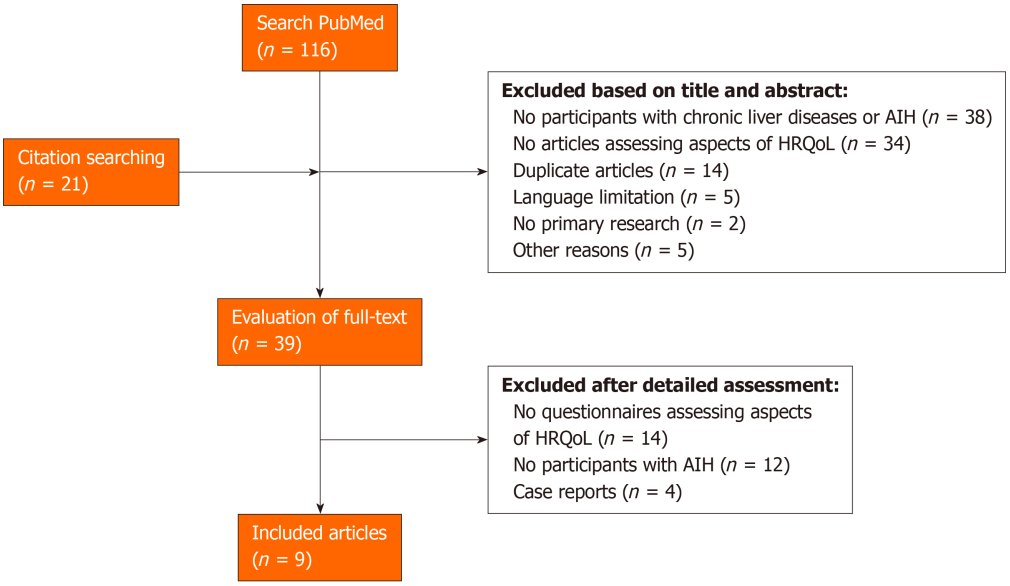

Figure 1 Flowchart of included studies after performing the literature search. AIH: Autoimmune hepatitis; HRQoL: Health-related quality of life.

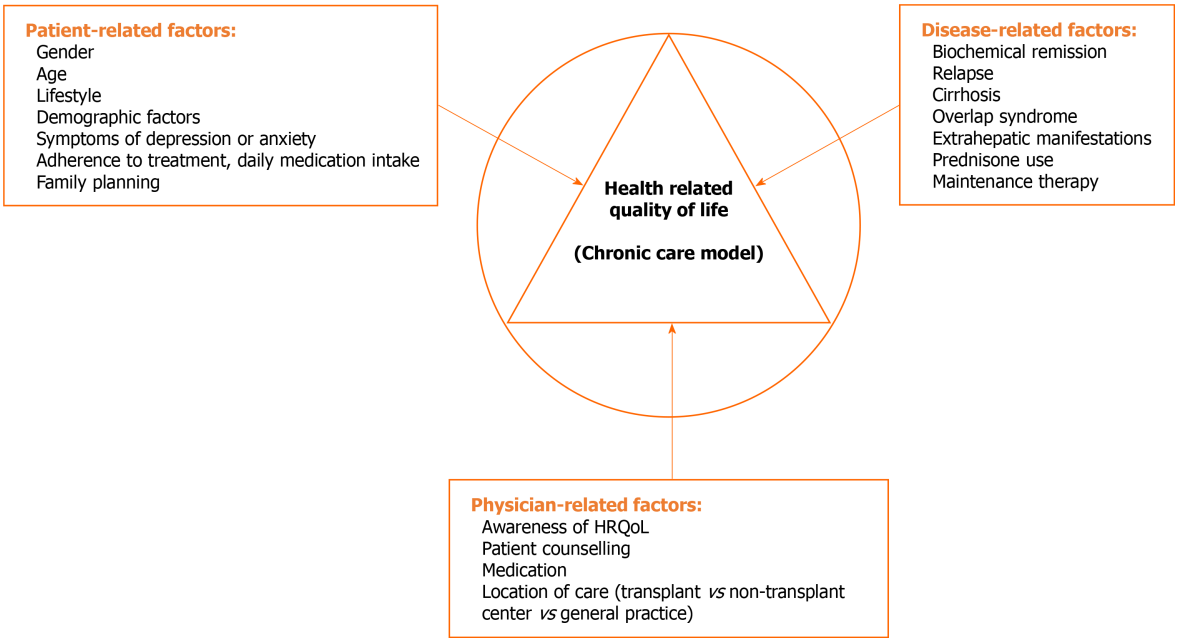

Figure 2 Patient-, disease- and physician-related factors affecting health-related quality of life in patients with autoimmune hepatitis. HRQoL: Health-related quality of life.

and anxiety symptoms, measured with the PHQ-9, GAD-7, or State-Trait Anxiety Inventory[12,15]. Depression was strongly correlated with both physical and mental components of SF-36. Despite biochemical remission in 77% of the patients (n = 103), the occurrence of severe depressive symptoms within the German cohort appeared to be five times as frequent compared with the general population.[12] In addition, even AIH patients without cirrhosis revealed more problems with regard to depression and anxiety compared with the general population[10]. It is interesting to note that psychological stress was also associated with relapses in patients with AIH type 1[20].

Other patient-related factors, particularly age and sex, have been described often in previous studies[7,11,12,14]. Studies in the United Kingdom and Japan reported a negative correlation between age and HRQoL[11,14], but Polish and Cuban studies did not find such a correlation [7,15]. With respect to sex differences, female patients experience more symptoms of depression[12,15] and have a worse quality of life than their male counterparts[7,15]. In our experience, women experience weight increase and other cosmetic changes associated with corticosteroids as a great inconvenience in

particular. In contrast, a study in the United Kingdom study found that the female sex was associated with a higher quality of life, albeit in an unadjusted regression analysis. These inconsistent correlations highlight that we still do not know which patient factors are important when assessing HRQoL in patients with AIH.

For all chronic liver diseases, it holds that lifestyle changes are part of the treatment. While tackling lifestyle is a hot topic in chronic disease, it is infrequently addressed in AIH. However, patients should still be informed about the risk of specific lifestyles, such as overweight, alcohol misuse, and sedentary behavior. Losing weight, more exercise, and a healthier diet contribute to successful management of chronic liver diseases and cirrhosis[21]. Indeed, exercising for more than 90 min/wk is a predictor of a better quality of life in patients with chronic liver diseases (*e.g.*, AIH)[7]. Another study confirmed that an increased body mass index was associated with a lower quality of life in patients with AIH[14]. In addition, alcohol consumption presents a clear risk of the progression of liver fibrosis in chronic liver diseases. Other factors, such as education level, socioeconomic data, smoking, or losing weight, were not frequently mentioned in the described studies. It follows that physicians need to communicate with patients about lifestyle adaptations through motivational interviews.

Coping with chronic conditions and taking medication daily goes hand in hand with discomfort, which potentially results in reduced HRQoL. Patients with more than one chronic disease that take daily medication have a lower quality of life[22]. Adherence to treatment is rarely discussed with patients but has a great impact on well-being and treatment response. A high psychosocial burden has been shown to significantly decrease adherence to treatment and to be associated with poor treatment response[23]. Therefore, prompt recognition of symptoms of depression and anxiety is important to improve patient adherence and lead to better response to treatment. Various factors may influence adherence to drug treatment in adolescents with AIH, particularly depression, anxiety, younger age, sex, prednisone dose, and long-term therapy have been found in previous studies[23-25]. In liver transplant recipients, marital status (if the patient is divorced) and having mental distress are associated with reduced self-reported adherence to immunotherapy[26]. However, information on demographic factors or socioeconomic data, including the status of a relationship and educational level, were not explicitly examined in all previous studies, which would be necessary for more detailed conclusions.

Disease-related factors

As mentioned previously, the main objective in treating AIH is to achieve complete biochemical and histological remission without side effects. While it is plausible that achieving biochemical remission results in better HRQoL, the association has not been studied often. One study found that patients with biochemical remission had a significantly higher quality of life [14]. One could speculate that incomplete biochemical remission causes uncertainty about, and possibly fear of, a relapse, which is understandable given that every relapse increases the risk of decompensated liver failure or the necessity of liver transplantation[27]. Whether this has a role in AIH is unknown at present.

Liver cirrhosis, or an advanced stage of fibrosis in patients with chronic liver disease is a known cause for reduced HRQoL, independent of the underlying liver disease[8, 28,29]. However, studies in patients with AIH demonstrate significant variability regarding the relation between fibrosis and HRQoL. Most studies describe that having liver fibrosis or compensated cirrhosis does not affect patient well-being in general[12, 14,15]. In contrast, another study did find an impaired physical condition in patients with AIH using the same SF-36 questionnaire and an overall lower quality of life using the CLDQ[11]. Plausible explanations for the discrepancy are the use of different general *vs* disease-specific, SF-36 *vs* SF-12 *vs* EQ-5D-5L questionnaires and the inclusion of different AIH populations regarding biochemical remission status and disease duration. Interestingly, none of the cited studies included AIH patients with decompensated cirrhosis in their cohort, which is known to be a major factor for reduced HRQoL in cirrhosis with other etiologies[30,31].

Patients with an overlap syndrome or a variant syndrome of AIH and primary biliary cholangitis (PBC) or primary sclerosing cholangitis (PSC), had a worse quality of life than patients not reporting those comorbidities[7,9,14]. In addition, fatigue is a typical symptom in patients with characteristics of PBC, and is expected to have a negative impact on HRQoL[7,9]. In that context, it is not only essential to treat both AIH and the overlapping syndrome (*i.e.*, PBC or PSC), but also to address associated symptoms (*i.e.*, IBD in PSC, itch in PBC) in the patients[14]. Interestingly, such a correlation was not found in a study in children with autoimmune liver diseases. It

found no differences in HRQoL scores in children with AIH *vs* overlap syndrome or variant syndrome with PSC[19]. Extrahepatic manifestations, for example thyroid disease, insulin-dependent diabetes mellitus, connective tissue disorders, and autoimmune skin disease, are common in AIH and can affect well-being, including fatigue, but the effect on HRQoL is unstudied so far[32].

A large proportion of patients with AIH receive corticosteroid therapy[11,33]. All treatments have specific side effects[34,35], but long-term use of corticosteroids is well-known for its undesirable effects, including osteoporosis, mood swings, depression, obesity, cognitive dysfunction, chronic fatigue, and reduced physical activity[1,5]. The negative impact of the use of corticosteroids on HRQoL was demonstrated in several studies[12,14]. In the United Kingdom cohort, corticosteroids were extensively linked to impaired HRQoL. Even patients who received low-dose of corticosteroids, and independent of their biochemical status, had a lower HRQoL[14]. Schramm *et al*[12] found a significant correlation between corticosteroids and depression. Sockalingam *et al*[23] found that patients with a moderate or high PHQ-9 score of > 10 were administered a significantly higher dose of prednisone compared with patients with a score of < 10. These data give additional support for steroid-free therapy as a treatment goal in every AIH patient to prevent steroid-related complications, and should be attempted within the first year of treatment. Other disease-related factors affecting mental well-being or HRQoL, such as markers of disease activity or disease duration, are so far unknown[12,15].

Currently, AZA is still the primary choice for maintenance therapy, and was not directly associated with a lower quality of life or health utility in a large cross-sectional analysis[14]. It is important to note that the use of AZA is associated with an increased risk of lymphoma and nonmelanoma skin cancer[36,37]. Although lymphoma in the long term is rare, it has to be taken into account that the occurrence of these side effects, or even the patient's concerns, might affect their quality of life. AZA may also cause hair loss that leads to alopecia. The possibility is frequently raised by the female patients and may affect various aspects of quality of life and lead to incompliance. The effect of other prescribed therapies on improving psychosocial outcomes, such as mycophenolate mofetil and mercaptopurine, is unknown. However, calcineurin inhibitors that have undesirable effects may be associated with lower health utility[14].

Physician-related factors

Physician-related factors are usually not addressed in studies and are thus difficult to take into account. Schramm *et al*[12] found that patient concerns about the severity of their disease, and being fearful of cirrhosis (mostly unnecessary) were factors associated with depression and anxiety symptoms. Providing the patient with information on his/her illness or medications and involving the patient in treatment options, can contribute to the patient's well-being. Whether the location of care (*i.e.* transplant *vs* nontransplant center) matters is uncertain. One study showed that there was no difference in health utility between transplant and nontransplant centers[14], and another found that biochemical remission rates were higher in transplant centers compared with nontransplant centers[33]. Both were conducted in the United Kingdom. Extrapolation of the results to other countries is difficult given the differences in health care management among countries.

CONCLUSION

It is clear that patients with AIH experience a lower quality of life and have more psychological problems, such as anxiety and depression, compared with the general population. Consistent evidence on which patient-related, disease-related, or physician-related factors cause HRQoL impairment in patients with AIH is lacking. Most studies did not include information on important socioeconomic, disease behavior, maintenance treatment, or even geographical factors, whereas they are known to affect patient well-being and HRQoL in other chronic liver diseases. In addition, some aspects of AIH are unexplored so far, for example the effect of lifestyle changes, extrahepatic manifestations, and patient counseling on HRQoL. Studies addressing HRQoL in pediatric AIH and their parents/support team are scarce and are desperately needed as a first step to improve their well-being.

Knowledge of HRQoL and associated factors in AIH are important to improve healthcare for AIH patients, for example by incorporating the factors in a chronic healthcare model (CCM). A CCM provides a clear approach for managing chronic diseases, with focus on assessment of the modifiable factors affecting the disease in

order to improve patient well-being. While no studies mentioned a CCM for AIH so far, some studies discussed elements that could be part of a model. For example, Janik *et al*[38] screened AIH patients for moderately severe depression and redirected them to a psychiatrist and psychiatric therapeutic interventions in case of a PHQ ≥ 15 points. Another example are lifestyle interventions for overweight patients[39]. There is also a role for the development of a disease-specific questionnaire for AIH patients, similar to the PBC-40 questionnaire, to measure the patient's perspective of the disease[40]. In what way, a CCM can be developed and implemented that would probably differ from country to country because of differences in health care. However, it is paramount that the AIH-specific CCM incorporate the most important factors of HRQoL in AIH, as discussed in this review.

Finally, HRQoL should not only be targeted in everyday clinical treatment approaches, but also as an important outcome of clinical trials and a research objective per se. Most studies of HRQoL in AIH have been conducted at a single center and comprised small numbers of patients, which underlines the need for collaboration between healthcare centers in different countries. Currently, there is an ongoing multicenter, cross-sectional study of HRQoL in patients with AIH within the European Network for Rare Liver Diseases. Recognizing the importance that quality of life has for the patient beyond the concept of biochemical and histological remission allows us to strive for significant improvements in management of adult and pediatric AIH.

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