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Fatigue in chronic liver disease: risk factors and treatment options

Submission date 04/11/2021	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 05/11/2021	**Overall study status** Completed	
Last Edited 02/09/2025	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Primary biliary cholangitis (PBC) is a type of liver disease that can get gradually worse over time. Fatigue is a common symptom and the major 'unmet need' in the management of patients with PBC. There are few prospective studies addressing the development of PBC-associated fatigue over time and the mechanisms underlying its development and maintenance are poorly understood. The aim of this study is to identify risk factors that determine the course and severity of fatigue in PBC.

Who can participate?
Adults from the age of 18 with a diagnosis of PBC or primary sclerosing cholangitis (PSC), a rare disease that attacks the bile ducts.

What does the study involve?
The associations and interactions between risk factors and fatigue will be assessed and compared in patients with PBC (a patient group severely affected by fatigue) and n= 240 patients with PSC (a group much less affected by fatigue). These variables will be monitored to identify factors that determine the severity and persistence of fatigue over time. An experimental study and interviews will be carried out in a sample of patients with newly diagnosed PBC. Their fecal microbiome (micro-organisms) will be analysed in order to find alterations in patients with high and low fatigue severity.

What are the possible benefits and risks of participating?
The study will investigate the natural course of fatigue in PBC (and PSC), and the study procedure will not influence patients´ regular medical treatment. Both patient groups receive 'care as usual' and there are no disadvantages for participants compared to non-participants. However, results will enhance the understanding of the causes of PBC fatigue and increase the knowledge on the predictive role of risk factors that are amenable to change. The study results will form a basis for future treatment and intervention approaches that aim to improve patients' quality of life.

Where is the study run from?
The study is being conducted by the YAEL - Center for Autoimmune Liver Diseases and the

Department of Psychosomatic Medicine and Psychotherapy, University Medical Centre Hamburg-Eppendorf, Germany. Microbiome analyses will be conducted in collaboration with the Institute of Clinical Molecular Biology (IKMB) of Kiel University (Germany).

When is the study starting and how long is it expected to run for?
May 2020 to September 2025

Who is funding the study?
Deutsche Forschungsgemeinschaft, DFG (German Research Foundation) (Germany)

Who is the main contact?
Prof. Dr med. Christoph Schramm, c.schramm@uke.de
Dr. phil. Anne Toussaint, a.toussaint@uke.de

Contact information

Type(s)
Scientific

Contact name
Dr Anne Toussaint

Contact details
Martinistraße 52
Hamburg
Germany
20246
+49 (0) 40 7410 - 52972
a.toussaint@uke.de

Type(s)
Scientific

Contact name
Prof Christoph Schramm

Contact details
Martinistraße 52
Hamburg
Germany
20246
+49 (0) 40 7410 - 52545
c.schramm@uke.de

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number
DFG grant numbers TO 908/3-1 and SCHR 781/7-1

Study information

Scientific Title
Fatigue in primary biliary cholangitis: factors associated with severity and persistence as future therapeutic targets

Acronym
SOMA.LIV

Study objectives
Hypotheses 1: Biomedical and psychosocial factors account for differences in fatigue experience between patients with primary biliary cholangitis (PBC) and primary sclerosing cholangitis.
Hypothesis 2: Biomedical risk factors (e.g. inflammatory cytokines, autonomic dysfunction) and psychological risk factors (e.g. depression, avoidance) predict the severity of fatigue among patients with PBC at 12-month follow-up, and their interplay determines its course over time.
Hypothesis 3a: Intestinal microbiota alterations are independently or conjointly with other biomedical and psychosocial factors associated with the severity of fatigue in patients with PBC.
Hypothesis 3b: Expectation of fatigue severity independently or conjointly with biomedical and psychosocial factors determines the severity of fatigue in patients with PBC.
Hypothesis 4: Higher anticipated fatigue prior to a stair-climbing task will correlate with worse performance and more severe post fatigue.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/01/2021, Ethics Committee of the Hamburg Medical Association (Ethik-Kommission der Ärztekammer Hamburg, Weidestraße 122 b, 22083, Hamburg, Germany; +49 (0) 40 202299-240; ethik@aekhh.de), ref: 2020-10196-BO-ff

Study design
Non-interventional prospective cohort study; mixed-methods design

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC)

Interventions
A prospective cohort study will be conducted in order to compare fatigue experience and related factors in patients with primary biliary cholangitis (PBC) and primary sclerosing

cholangitis (PSC). Using a mixed-methods approach, the role of symptom perception and expectations in the development and maintenance of fatigue will be further examined in a subgroup of newly diagnosed patients with PBC.

Prospective cohort study:
In the prospective cohort study, the natural course of fatigue in patients with PBC compared to PSC (a control cholestatic liver disease group much less affected by fatigue) will be investigated. Follow-up measurements will take place after 6 and 12 months. Patient data will be collected through self-report questionnaires, semi-structured interviews, and blood and stool samples.

Experimental study:
In an experimental study, a subgroup of newly diagnosed patients with PBC will rate their momentary fatigue and anticipated fatigue prior to a self-paced stair-climbing task. After the task, they will re-rate experienced fatigue.

Qualitative study:
Qualitative interviews will be conducted in the subsample of newly diagnosed patients in order to complement the quantitative data. Patients will undergo semi-structured interviews before their first medical consultation at the YAEL - Center, and at 6- and 12-month follow-up. Interview questions will assess patients' symptom perception, management strategies, causal attributions and expectations on fatigue.

Microbiome analysis:
Shotgun metagenomic sequencing will be performed in order to identify bacterial species and functional annotations in patients with PBC and PSC, and high versus low fatigue scores, respectively.

Intervention Type
Other

Primary outcome(s)
The severity of fatigue assessed using the Fatigue Visual Analogue Scale (Fatigue-VAS) score and the Primary Biliary Cirrhosis-40 (PBC-40) fatigue domain score at baseline, after 6 months, and after 12 months

Key secondary outcome(s))
1. Total somatic symptom severity measured using the Patient Health Questionnaire-15 (PHQ-15) at baseline, 6 months, and 12 months
2. Symptom intensity measured using a Numeric Rating Scale (NRS) at baseline, 6 months, and 12 months
3. Pruritus severity measured using a Numeric Rating Scale (NRS) at baseline, 6 months, and 12 months
4. Symptom interference with daily activities using a Numeric Rating Scale (NRS) at baseline, 6 months, and 12 months
5. Symptom-related disability measured using the Pain Disability Index (PDI) at baseline, 6 months, and 12 months
6. General mental and physical quality of life measured using the Short-Form Health Survey (SF-12) at baseline, 6 months, and 12 months
7. Disability-specific quality of life measured using the respective subdomain of the Primary Biliary Cirrhosis-40 (PBC-40) at baseline, 6 months, and 12 months

Completion date
30/09/2025

Eligibility

Key inclusion criteria
1. Clinical diagnosis of PBC (PSC)
2. Sufficient oral and written German language proficiency
3. Provision of written consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
480

Key exclusion criteria
1. Advanced cirrhosis (Child Pugh score ≥8)
2. Decompensated liver disease (autoimmune hepatitis or chronic viral hepatitis B or C)
3. Clinically significant untreated intercurrent medical condition associated with fatigue (i.e. hypothyroidism, anaemia, fibromyalgia, rheumatoid arthritis, systemic lupus erythematosus and manifest depression)
4. Antibiotic treatment during the past 6 weeks (exclusion only in microbiome study)
5. Ongoing participation in clinical trials on fatigue
6. Intercurrent active or latent infection
7. Florid psychosis
8. Substance abuse disorder
9. Acute suicidality

Date of first enrolment
21/03/2022

Date of final enrolment
31/12/2023

Locations

Countries of recruitment
Germany

Study participating centre
University Medical Centre Hamburg-Eppendorf
YEAL-Center for Autoimmune Liver Diseases
Martinistraße 52
Hamburg
Germany
20246

Study participating centre
University Medical Centre Hamburg-Eppendorf
Department of Psychosomatic Medicine and Psychotherapy
Martinistraße 52
Hamburg
Germany
20246

Study participating centre
Christian-Albrechts-University Kiel
Institute of Clinical Molecular Biology
Rosalind-Franklin-Straße 12
Kiel
Germany
24105

Sponsor information

Organisation
University Medical Center Hamburg-Eppendorf

ROR
https://ror.org/01zgy1s35

Funder(s)

Funder type
Charity

Funder Name
Deutsche Forschungsgemeinschaft

Alternative Name(s)
German Research Association, German Research Foundation, Deutsche Forschungsgemeinschaft (DFG), DFG

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Germany

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a publically available repository (e.g., DRYAD Digital Repository; https://datadryad.org/stash). The study protocol and statistical analysis plan will be available at the ISRCTN registry. Individual participant data that underlie the reported results in a published article will be shared after de-identification beginning 3 months and ending 5 years following article publication. Data will be shared with researchers who provide a methodologically sound proposal to achieve the aims in the approved proposal. Proposals should be directed to Dr Anne Toussaint (a.toussaint@uke.de). To gain access, data requestors will need to sign a data access agreement. Informed consent from participants was obtained.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		07/12/2022	06/01/2023	Yes	No
Participant information sheet	version 2	17/01/2021	05/11/2021	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes