

Depression in patients with autoimmune hepatitis: the need for detailed psychiatric assessment

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Introduction Autoimmune hepatitis (AIH) is a progressive liver disease, occurring more frequently in women, which, if left untreated, leads to cirrhosis and hepatic failure.¹ Current therapies are based on long-term immunosuppression, which induces remission in the majority of patients; however, the risk of subsequent relapses is high. Treatment adherence is one of the crucial factors for achieving clinical success.²

Recent studies have demonstrated that patients with AIH have a substantially diminished health-related quality of life.³⁻⁵ In particular, depression has emerged as an underestimated factor affecting the well-being of patients with AIH.⁶ Unfortunately, depression is rarely assessed in everyday clinical practice. The Patient Health Questionnaire-9 (PHQ-9) and the Hospital Anxiety and Depression Scale (HADS) are simple screening tools that are successfully applied in patients with AIH and indicate those who need further evaluation. However, they do not permit a precise assessment of the condition. Indeed, to diagnose depression, assessment of the following is necessary: etiology of depression, duration of symptoms, disease's impact on daily activities, psychiatric history, and other factors that are not considered in the screening tools.

Given the above, we performed an extended psychiatric assessment, which involved a detailed psychiatric evaluation, a battery of screening tests, and a structured interview (the Mini-International Neuropsychiatric Interview [M.I.N.I.]), focusing on patients with AIH who previously presented the highest scores on a depression screening test in our center.

Patients and methods We prospectively assessed adult patients with AIH from our previous study⁵ who had screened positive for moderately severe depression (>15 points in the PHQ-9). According to Levis et al,⁷ this cut-off value allows to exclude major depression in 96% of patients. None of the included patients had signs of decompensated liver cirrhosis, hepatic encephalopathy, malignancies, previously diagnosed psychiatric disorders, or complained of adverse effects of drugs for AIH. The study flow chart is presented in **FIGURE 1**.

Psychiatric assessment The psychiatric assessment comprised of a psychiatric consultation (documented with a standard psychiatric consultation note in the format recommended by the Massachusetts General Hospital)⁸ and a battery of validated tests, namely the Alcohol Use Disorders Identification Test (AUDIT), the Generalized Anxiety Disorder-7 (GAD-7) scale, which were included in the Stanford Integrated Psychosocial Assessment for Transplant (SIPAT) final score, and the M.I.N.I.

Generalized Anxiety Disorder-7 The GAD-7 scale, stemming from the Primary Care Evaluation of Mental Disorders screening tool, is a self-administered screening test for core anxiety symptoms, primarily designed as a measure to screen for generalized anxiety disorder, but also having sufficiently good operating characteristics for 3 other anxiety disorders: panic disorder, social anxiety disorder, and posttraumatic stress disorder.⁹ The severity of anxiety is assessed by

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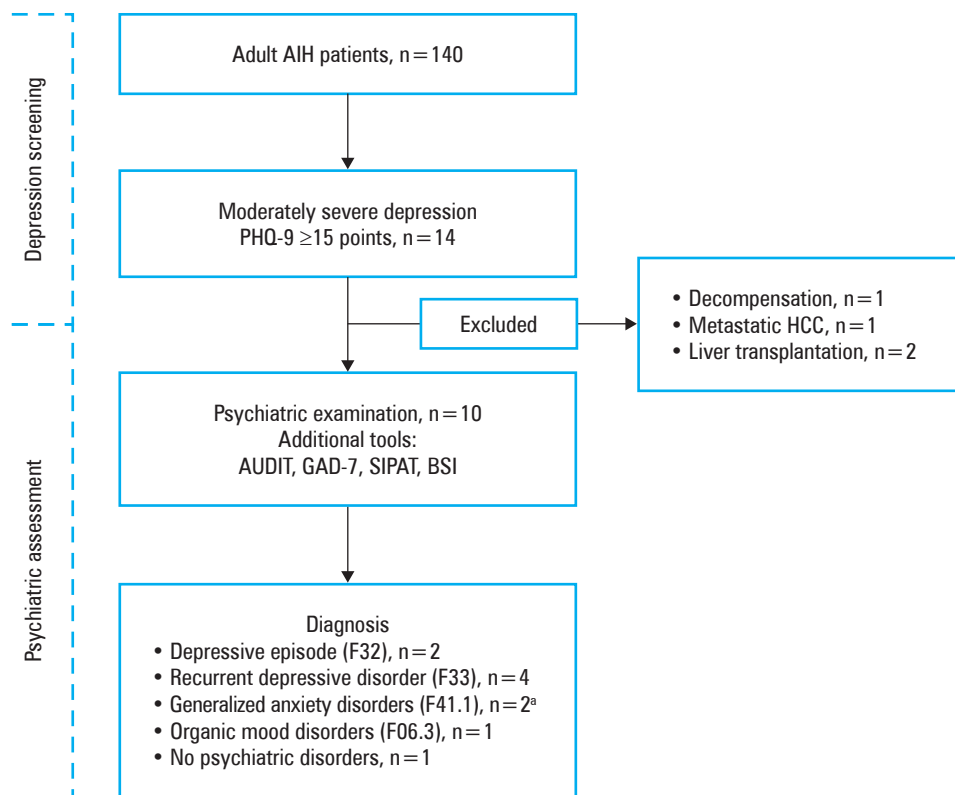
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FIGURE 1 Study flow chart. The diagnosis codes according to *International Classification of Diseases, Tenth Revision (ICD-10)* were provided in parentheses. **a** Comorbidities diagnosed according to *ICD-10* in 2 patients: 1 with F33 and 1 with F32. Abbreviations: AIH, autoimmune hepatitis; AUDIT, Alcohol Use Disorders Identification Test; BSI, Brief Symptom Inventory; GAD-7, Generalized Anxiety Disorder-7; HCC, hepatocellular carcinoma; PHQ-9, Patient Health Questionnaire-9; SIPAT, Stanford Integrated Psychosocial Assessment for Transplantation



assigning 0, 1, 2, or 3 to the response categories “not at all,” “several days,” “more than half of the days,” and “nearly every day,” respectively, with a total score ranging from 0 to 21. The recommended cut-off point for further evaluation is a score of 10 or greater.⁹

The Mini-International Neuropsychiatric Interview The M.I.N.I. is a structured psychiatric interview developed by Sheehan et al,¹⁰ which allows for making a psychiatric diagnosis according to *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) and the psychiatric criteria included in *International Classification of Diseases, Tenth Revision* and provides good accuracy and reliability in this aspect.

Alcohol Use Disorders Identification Test The AUDIT was used to exclude alcohol use disorders overlapping with depressive symptoms, anxiety, and liver dysfunction.¹¹ Although patients with AIH are not commonly diagnosed with alcohol abuse or dependence, some of them are not committed to complete abstinence after being diagnosed with AIH, which may shape the course of the disease and influence psychiatric symptoms, and a differential diagnosis should be documented. The AUDIT is a 10-item tool developed by the World Health Organization to assess alcohol consumption, drinking behaviors, and alcohol-related problems. Patients are also encouraged to define their alcohol intake measured objectively with the amount of standard drinks consumed by them. A total score of 8 or more is considered to indicate hazardous or harmful alcohol use.

Stanford Integrated Psychosocial Assessment for Transplant The SIPAT scale was developed by Maldonado

et al¹² as a complex and comprehensive tool that integrates the assessment of a patient’s understanding of the disease, adherence, social support, and readiness for treatment as well as screening for psychiatric risk that includes the stratified PHQ-9 (alternatively the Beck Depression Inventory), the GAD-7 scale, the Mini-Mental State Examination, the AUDIT scale, and screening for problems related to the use of illicit drugs. The scale allows to stratify potential liver transplant recipients into excellent, good, minimally acceptable, poor, and high-risk candidates, but also suggests recommendations for remediation measures and reassessment.

Clinical evaluation Routine liver function tests and liver stiffness measurements were performed with the real-time 2-dimensional shear wave elastography. The diagnosis of cirrhosis was based on the results of histologic examination, elastography, and / or imaging studies. The local ethics committee approved the study protocol (KB/128/2015), and written consent was obtained from all participants.

Statistical analysis The data were presented as mean (SD) and / or median values and ranges, when appropriate for continuous variables. The Kolmogorov–Smirnov normality test was used to examine the distribution of quantitative variables, which revealed a nonparametric distribution. The data were analyzed with the Statistica software, version 13 (Dell Inc., Tulsa, Oklahoma, United States).

Results The screening test results of 14 patients, who comprised 10% of the total number of 140

patients included into our previous study,⁵ suggested moderately severe depressive symptoms. Four patients were excluded from the further analysis: 1 had developed decompensated liver disease, 1 was diagnosed with hepatocellular carcinoma, and 2 had undergone transplantation before their psychiatric assessment. The clinical data and results from the psychiatric evaluation are presented in the Supplementary material (*Table S1*). None of the patients had a flare of AIH. The detailed psychiatric consultations revealed a positive diagnosis of depression (present, past, or recurrent) in 6 patients (60%) as well as anxiety- or stress-related disorders in 2 patients (20%). Finally, 6 patients (60%) were advised to take antidepressants (selective serotonin or serotonin and norepinephrine reuptake inhibitors) and scheduled for a psychiatric follow-up. It is worth noting that 9 patients had never sought psychiatric assistance before. Interestingly, 2 patients who had undergone liver transplantation and were excluded from the cohort had no signs of depression in the follow-up period but were diagnosed with adjustment disorders (*ICD-10*, F43.2).

Discussion To the best of our knowledge, this is the first study which estimates the prevalence of depression in patients with AIH with a full psychiatric evaluation. We performed a thorough psychiatric assessment of patients who screened positive for moderately severe depression in a simple and commonly used questionnaire – the PHQ-9. This assessment showed that 6 out of 10 patients had depression requiring medical therapy. Two of them were diagnosed with one or more anxiety- or stress-related disorders as comorbidities. These results are in line with the recently published meta-analysis, which showed that a higher cut-off value of the PHQ-9 (eg, >15 points) could accurately rule out patients with major depression, but could also indicate a false-positive result in 39% of the patients screened positive.⁷ The results of a detailed psychiatric interview confirmed this false-positive rate using a higher cut-off point of the PHQ-9 in the AIH setting. A lower specificity of the PHQ-9 was reported in younger populations,⁷ which corresponds well with our cohort of patients and may have affected the final results.

These findings suggest that the currently available screening methods might not be adequate for estimating the real extent of depression and other psychiatric disorders in patients with AIH. They could also explain the discrepancy in the results of positive screening for depression in cohorts described in available literature, which range from 5.5% to 29%, depending on the cohort.⁶

Overall, the results presented herein further underscore the fact that presumed depression, detected with basic screening modalities, calls for special attention in patients with AIH. It should be thoroughly followed since a therapeutic intervention may be required in the majority of the identified patients. This is of particular importance to younger patients as depression affects

not only their well-being but also adherence to treatment. The latter may have a detrimental impact on the outcome of therapy.² To accomplish this task, a close cooperation between hepatologists and psychiatrists is needed and, equally important, dedicated screening tools should be developed and validated in the near future.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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