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SCREENING AND MANAGEMENT OF PSYCHIATRIC DISORDERS IN PATIENTS WITH WILSON'S DISEASE

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Summary:

Hepatomegaly is an autosomal recessive condition with an estimated 1:30000 cases worldwide. Because the symptoms and indicators of hepatomegaly mental disease are poorly understood, the ailment is frequently misdiagnosed or underdiagnosed, which causes irreparable nerve damage in the patient's later years. To comprehensively review the research and offer a list of treatments for treating mental illnesses in hepatomegaly. PRISMA guidelines were used to deliver the review. Evidence-based nursing standards were used to design research questions and tactics. In order to find information on hepatomegaly clinical guidelines, systematic reviews, randomized controlled trials (RCTs), and expert consensus on the management of mental disorders in patients with nuclear degeneration, all databases of CINAHL, Up to Date, the Cochrane Library, Pubmed(Medline), Embase, Wiley, JBI, International Guidelines.com, Wanfang, and CNKI were searched. This investigation covered a total of 14 publications, and 41 best evidence items, encompassing screening, evaluation, clinical symptoms, pharmaceutical therapies, non-pharmacological interventions, and health education, were retrieved. It is recommended that healthcare professionals evaluate our cultural characteristics, medical resources, and patient's subjective and objective conditions before clinical application, apply the evidence in a targeted manner to improve patient's health outcomes, and reduce readmissions. The 41 best evidence for patients with hepatomegaly can guide the treatment and rehabilitation of patients with hepatomegaly and psychiatric disorders.

Keywords:*Hepatomegaly;Mental Disorders; Screening; Management; Evidence to summarize*

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INTRODUCTION

A main impairment of copper metabolism characterizes the autosomal recessive condition hepatomegaly (Liu et al.2017). The condition affects people of various ages, with the majority first showing symptoms between the ages of 5 and 35. The disease can now be diagnosed in people as young as 3 years old and as old as 80. (Yang et al.2012). The prevalence in the general population is 1/30,000 to 1/100,000, with a 1/90 carrier rate for the causal gene and a 25% to 50% positive family history (Jia et al. 2013). Chinese populations have a higher incidence than those in Europe and America (Liang 2009).

The ATP7B gene mutation at 13q14.3 causes reduced or absent ATPase activity, insufficient serum copper blue protein synthesis, decreased biliary copper excretion, and lysosomal dysfunction. The liver, kidney, cornea, bone marrow, and basal ganglia of the brain are among the organs damaged by the body's amassed free copper ions when they join with histones and are deposited there. This damage results in progressive cirrhosis, extrapyramidal symptoms, and corneal damage. As a result, there is severe cirrhosis, renal damage, extrapyramidal symptoms, corneal pigmentation rings (K-F rings), and psychiatric problems. Some people display psychiatric illnesses to varied degrees, frequently in conjunction with somatic symptoms. The typical signs of mental illness are affective problems, particularly emotional instability, euphoria, stubbornness, irritation, diminished initiative, uncoordinated emotional reactions, and strange conduct (Yang et al. 2012, Li et al. 2020).

Nearly all hepatomegaly patients eventually have psychological problems if they go untreated. To ensure that patients with hepatomegaly can be treated successfully, timely and comprehensive interventions with high-quality care are required. Treatment that is given too late is typically useless. But because people are ignorant of the symptoms and signs of hepatomegaly, the disorder is frequently misdiagnosed or underdiagnosed, which worsens later-life irreversible brain damage (Xu et al. 2013). The symptoms of mental problems secondary to alternative metabolic abnormalities brought on by liver failure may also result in more severe or advanced diseases, according to doctors (Zhang & Hu 2013). The incidence of drug-related complications, readmission rates, and patient quality of life can all be significantly reduced by pre-symptomatic screening and diagnosis of patients, scientific and standardized symptomatic treatment after diagnosis, and the development of the best evidence-based refinement of symptom management in patients with hepatomegaly.

Unfortunately, there is still limited domestic research on the most effective hepatomegaly management

strategies. Researchers have looked into a number of crucial facets of screening, assessment, and health education, but no comprehensive approach has been developed. As a critical component of improving patient health outcomes and a pressing need to address the current situation of managing hepatomegaly symptoms, they are synthesizing domestic and international research results and summarizing the best evidence on managing mental disorders in patients with hepatomegaly.

This study analyses the high-quality literature for evidence-based therapy in the management of mental diseases in patients with hepatomegaly in order to provide direction for therapeutic care and rehabilitation of patients with hepatomegaly.

METHODOLOGY

Establishment of the problem

The PIPOST model of the JBI Evidence-Based Health Care Center's question generation tool was utilized in this study to create the initial questions for the management of mental illnesses in patients with hepatomegaly (Aromataris et al.2015). P (population) stands for persons with mental problems who have hepatomegaly. P (implementer): medical professionals and nurses; I (intervention): data pertaining to the care of mental problems in patients with hepatomegaly, such as screening and evaluation tools for mental disorders and related health education; O (outcome): The incidence of mental illnesses, remission rates, and readmission rates in patients with hepatomegaly are the primary outcome indicators; secondary outcome indicators include the level of medical staff members' familiarity with patients' mental disorders and the creation of a process for managing mental disorders; hospital S (site); Guidelines, evidence summaries, expert consensus, systematic reviews, meta-analyses, high-quality randomized controlled trials, etc. are all examples of T (type of evidence).

Evidence source and retrieval strategies

A top-down literature search was conducted using the "6S" evidence search model(Hu & Hao 2017). When searching the guideline library and government websites, the search terms were "hepatolenticular degeneration/ Wilson's disease/hepatolenticular degeneration/Wilson disease/hepatomegaly/assessment/prevention/management/ treatment/care/nursing" with the phrase National Institute for Health and Care Excellence (NICE), Guideline International Network (GIN), World Health Organization website, Ontario Nursing Society website, Google, BMJ Best Practice, Up To Date, Medical Pulse Clinical Guidelines, National Health Council.

A combination of subject terms and free words were used to search domestic and international databases. The search terms were "hepatolenticular degeneration/ Wilson's disease/hepatolenticular degeneration/Wilson disease/hepatomegaly/assessment/prevention/management/treatment/care/nursing" from JBI Center for Evidence-Based Health Care, Pubmed, CINAHL, Embase, Medline, OVID, Wiley, The Cochrane Library, CNKI, VIP, and Wanfang Data. The search time limit is from establishing the database to July 21, 2022.

Literature inclusion and exclusion criteria

To be eligible for inclusion in this study, the articles had to meet the following inclusion criteria: Inclusion criteria: (I)study population: patients diagnosed with hepatomegaly mental disorder; (II) study content related to screening, assessment, diagnosis, care, management, and prevention of patients with hepatomegaly; (III) type of literature: guidelines, best practice information booklets, systematic evaluations and Meta-analyses, expert consensus, high-quality randomized controlled trials, and clinical decisions; (IV)language of the publication was limited to Chinese or English.

Articles were excluded from the study if they met any of the following exclusion criteria: (I)incomplete information; (II)translated and simplified versions of guidelines or updated versions available; (III)failed methodological quality evaluation of the literature; (IV) conference reports, drafts, plans, etc.

Literature quality evaluation criteria

Based on the type of literature, the appropriate evaluation criteria were selected for quality evaluation. Guidelines included in this study were evaluated for quality using the 2017 edition of the Clinical Guidelines Research and Evaluation System (AGREE II)(Hoffmann-Eßer et al.2017). The systematic evaluation and expert consensus for inclusion in this study was evaluated for quality using the JBI Center for Evidence-Based Health Care's Literature Research Evaluation Tool (2016 version) accordingly. Evidence summaries were traced back to the original literature, and the corresponding methodological quality evaluations were performed according to the specific type of original literature.

Literature quality evaluation process

Two researchers with experience in evidence-based nursing independently assessed the literature's quality. A research team made up of nursing management, encephalopathy-trained nurses, and encephalopathy-trained doctors debated whether to incorporate contentious literature internally before coming to a consensus. This study followed the guidelines of prioritization of the most recent published evidence, evidence-based evidence, and high-quality evidence when the outcomes of various literature searches were inconclusive.

RESULTS

General characteristics of the included articles

Preliminary searches of various official websites and databases yielded a total of 642 publications. The remaining 34 publications were read in full after duplicate works and works having little connection to the subject of this study were eliminated. Two researchers read the remaining literature in its entirety, and after evaluating the methodological quality of the literature that complied with the criteria, 14 papers – including seven guidelines, one clinical decision, one clinical trial, three expert consensuses, and two systematic evaluations – were ultimately included. Figure 1 depicts the process flow for the literature screening, and Table 1 provides general information about the literature that was included.

Quality evaluation results of the included literature

Effects of quality evaluation of the guidelines

Seven guidelines were included in this study, of which one approach was from NICE, three from Medical Pulse, and three from Pubmed. According to the AGREEll recommendation criteria, five guidelines(European Association for Study of Liver.2012,Nagra et al.2018, the Neurogenetics Group of the Chinese Society of Neurology 2021,the Chinese Society of Branch of Liver Diseases 2022,Shribman et al.2022), with standardization percentages ≥ 60% in six domains were recommended at level A. The remaining guidelines were recommended at level B. The specific evaluation results are shown in Table 2.

Results of the quality evaluation of expert consensus and clinical decisions

One clinical decision(Schilsky et al.2021)was included in this study, and the level of literature was high enough to be used directly in this study. Three expert consensuses were included in this study, one from Pubmed, one from Wiley, and one from Google. According to the evaluation criteria, one medium-quality literature(Hepatology and Nutrition 2018)and two high-quality literature(Ferenci et al.2003,Litwin et al.2019), with a complete study design and high overall quality, were included, and the specific evaluation results are shown in Table 3.

Quality evaluation of systematic evaluations

Two systematic evaluations were included in this study, one(Zimbrean & Schilsky 2014) from Google and one (Mulligan & Bronstein 2020) from Pubmed. The study design was more complete and of higher overall quality and was included, as shown in Table 4.

Quality evaluation of clinical trials

One trial was included in this study (Tampakia et al.2020)from the OVID database, in which all entries were evaluated as "yes" except for entry 5, which was assessed as "no", and the trial design was complete and high quality, and was included.

Summary of evidence

Extraction of the final included studies yielded 41 pieces of relevant evidence, as shown in Table 5. All included evidence was graded using the Australian JBI Centre for Evidence-Based Medicine evidence recommendation rating system. Evidence obtained from the evidence summary was graded retrospectively to the original literature, the FAME attribute of each evidence was screened. The evidence grade was classified as Level 1 to 5 according to the design type of the evidence. Based on the JBI recommendation grading, the recommended grade of the evidence was determined as Level A or Level B.

Table 1 Characteristics of the included literature

Included articles	Topic of the article	Development of the organization	Type of evidence	Year	Source
European Association for Study of Liver.	Diagnosis, treatment and prevention of Wilson's disease	European Liver Association	Clinical guideline	2012	NICE
Nagra et al.	Integrated management of hepatic, neurological and psychiatric disorders in Wilson's disease	National Society for the Study of Liver Diseases, India / Indian Society of Paediatric Gastroenterology, Hepatology and Nutrition / Indian Society of Movement Disorders	Clinical guideline	2019	YiMai Tong
Neurogenetics Group of the Neurology Branch of the Chinese Medical Association	Chinese guidelines for the diagnosis and treatment of Wilson's disease	Neurogenetic Diseases Group of the Chinese Medical Association, Neurology Branch	Clinical guideline	2021	YiMai Tong
Medici et al.	A practical approach to the diagnosis, treatment and follow-up of Wilson's disease	—	Clinical guideline	2007	CINAHL
Roberts et al.	Diagnosis and treatment of Wilson's disease	American Association for the Study of Liver Diseases	Clinical guideline	2008	Wiley
Socha et al.	Diagnosis, treatment and follow-up of Wilson's disease in children	European Society for Pediatric Gastroenterology, Hepatology and Nutrition and Committee on Liver Diseases	Expert consensus	2018	Pubmed
Ferenci et al.	Diagnosis and phenotypic classification of Wilson's disease	European Liver Association	Expert consensus	2003	Wiley
Litwin et al.	Current status and new advances in the treatment of Wilson's disease	Institute of Psychiatry and Neurology, Warsaw, Poland; Department of Neurology and Center for Clinical Neuroscience, First Medical School and General University Hospital, Prague, Czech Republic	Expert consensus	2019	Google
Zimbrean et al.	Review of the evidence on psychiatric symptoms of Wilson's disease	—	Systematic review	2014	Google
Mulligan et al.	Overview of Wilson's disease and disease management approaches	—	Systematic review	2020	Pubmed
Michael et al.	Clinical presentation and diagnosis of Wilson's disease	—	Clinical decision	2021	Up to date
Tampakia et al.	Epidemiological history of Wilson's disease over the past 30 years	—	RCT	2020	Pubmed
Chinese Medical Association, Hepatology Branch	Guidelines for the treatment of Wilson's disease	Collaborative Group on Inherited Metabolic Liver Diseases, Chinese Medical Association, Hepatology Branch	Clinical guideline	2022	YiMai Tong
Shribman et al.	Evaluation, diagnosis and therapeutic management of Wilson's disease	British Hepatology Society	Clinical guideline	2022	Pubmed

Table2 Quality assessment results of included guidelines

Included literature	Standardized scores in each area(%)						Field number (n)		Recommendation level
	Scope and purpose	Involved personnel	Preciseness of guideline Development	Clarity of Presentation	Applicability	Independence of writing	≥ 60%	30% ~60%	
Saroli et al.	97.25	86.73	83.21	95.46	87.50	67.83	6	0	A
Nagra et al.	94.73	78.87	67.83	91.67	83.22	39.36	5	1	A
Neurogenetics Group of the Neurology Branch of the Chinese Medical Association	95.27	77.69	55.62	88.86	69.75	46.75	4	2	A
Medici et al.	83.27	59.00	43.51	77.98	58.44	33.21	3	3	B
Roberts et al.	75.41	37.78	47.45	79.67	54.68	89.73	3	3	B
Chinese Medical Association, Hepatology Branch	96.00	75.44	56.43	85.77	64.35	81.64	5	1	A
Shribman et al.	97.30	71.25	47.67	83.23	78.27	58.60	5	1	A

Table 3 Quality evaluation results of the inclusion of expert consensus

Included literature	1	2	3	4	5	6
Socha et al.	Yes	Yes	Yes	Unclear	Yes	No
Ferenci et al.	Yes	Yes	Yes	Yes	Yes	No
Litwin et al.	Yes	Yes	Yes	Yes	Yes	No

Note: **1** whether the source of the viewpoint is clearly marked; **2** whether the viewpoint comes from influential experts in the field; **3** whether the viewpoint presented is centered on the interests of the population concerned by the study; **4** whether the stated conclusion is based on the results of the analysis and whether the viewpoint is expressed logically; **5** whether reference is made to other existing literature; **6** whether the viewpoint presented is inconsistent with previous literature.

Table 4 Quality assessment results of included systematic reviews

Included literature	1	2	3	4	5	6	7	8	9	10	11
Zimbrean et al.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes
Mulligan et al.	Yes	Yes	Yes	Yes	Unclear	Yes	No	Yes	Yes	Yes	Yes

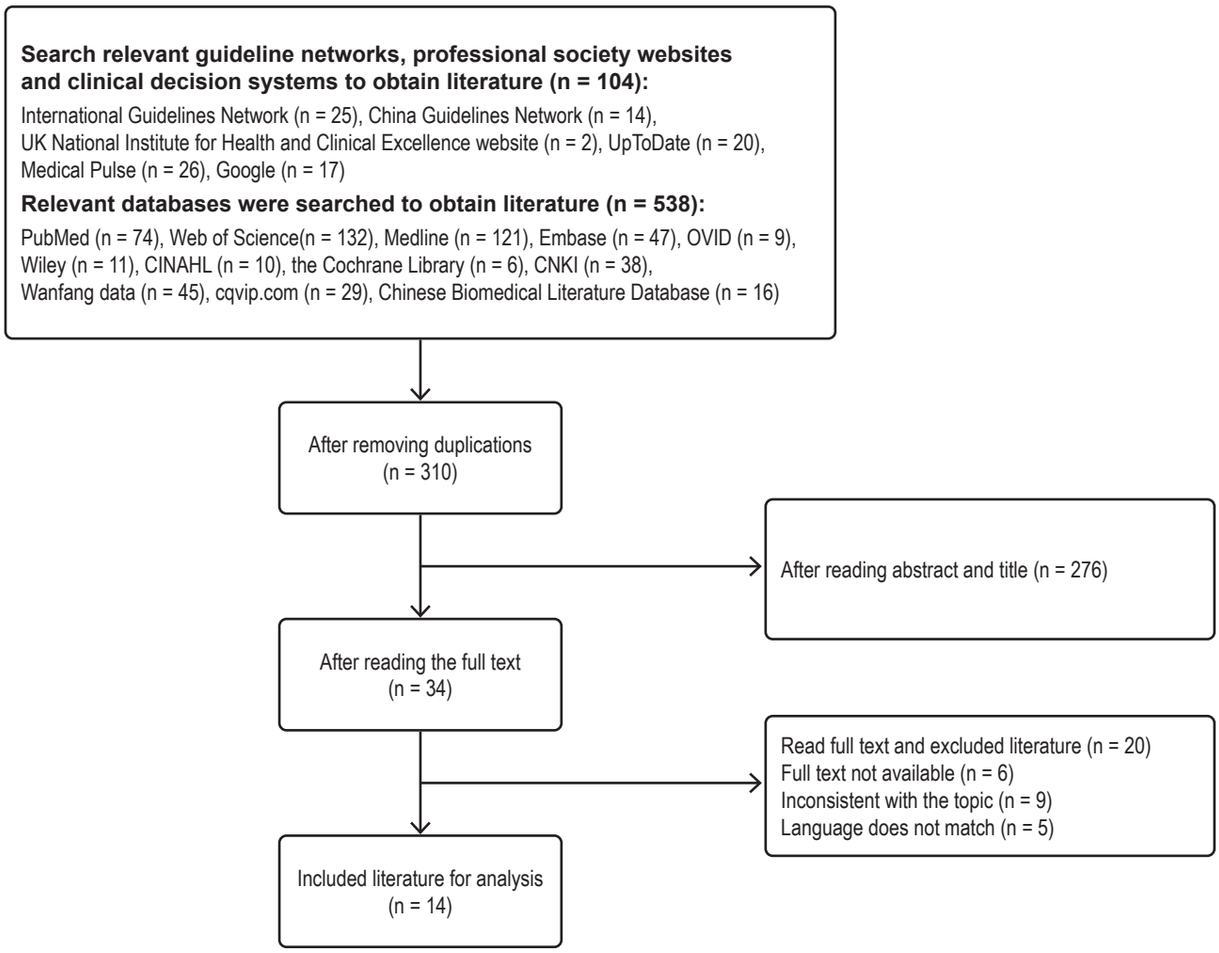
Note:**1** whether the evidence-based questions were clear and explicit; **2** whether the literature inclusion criteria were appropriate; **3** whether the search strategy was appropriate; **4** whether the literature sources were appropriate; **5** whether the literature quality evaluation criteria were appropriate; **6** whether the literature quality evaluation was done independently by two or more evaluators; **7** whether measures were taken to reduce errors in data extraction; **8** whether the study merging method was appropriate; **9** whether publication bias was assessed; **10** whether the proposed Whether the recommendation is based on the results of systematic evaluation; **11** whether the proposed further research is appropriate.

Table 5 Summary of best evidence for the management of patients with mental disorders in Wilson's disease

Category	Evidence content	Evidence level	Recommendation level
Screening	Screening subjects (European Association for Study of Liver.2012,Socha et al.2018,Ferenci et al.2003,Litwin et al.2019,Michael et al.2021,Tampakia et al.2020,Chinese Medical Association, Hepatology Branch.2022): patients with psychiatric symptoms of unknown origin should be considered for the possibility of WD	I a	A
	Screening subjects(Nagra et al.2019,Tampakia et al.2020): adolescents with unexplained cognitive impairment and psychiatric disorders should be excluded from having WD	I a	A
	Screening tools (European Association for Study of Liver.2012,Michael et al.2021): patients with suspected WD should be examined by the clinician for K-F ring. In patients with neuropsychiatric abnormalities, the absence of K-F ring also does not exclude WD.	I b	B
	Screening indicators(Nagra et al.2019,Litwin et al. 2019,Zimbrean et al.2014,Tampakia et al.2020,Chinese Medical Association, Hepatology Branch.2022): Leipzig criteria, Ferenci score, serum free copper concentration, hepatic copper concentration, 24-h urinary copper excretion, plasma copper cyanine concentration, Kayser-Fleischer ring, genetic testing	I a	A
	Once patients are diagnosed with WD, they should be screen -ed by their first-degree relatives(Nagra et al.2019,Neurogenetics Group of the Neurology Branch of the Chinese Medical Associa -tion.2021,Medici et al.2007)	I a	A
	All mixed movement disorders combined with behavioral or personality changes or any other red flags should be screened for WD routinely and expanded, and neuropsychiatric imaging should also be performed (Shribman et al.2022)	I c	B
	Because of the risk of worsening neuropsychiatric symptoms, initial workup should be refined as soon as possible (Shribman et al.2022)	I c	B
Assessment	MRI of the brain can be used as a means of assessing the condition and monitoring the efficacy of treatment in patients with neuropsychiatric pathology WD(Ferenci et al.,2003;Chinese Medical Association, Hepatology Branch.2022,Shribman et al.2022)	I a	B
	Serum copper blue protein should be routinely measured in the evaluation of unexplained psychiatric abnormalities in children and adults to middle age(Litwin et al.2019,Mulligan et al.2020)	I a	B
	Mental disorders can occur at any point in the course of WD, including in the absence of liver or neurological lesions(Roberts et al.2008,Tampakia et al.2020)	I b	A
Clinical manifestations	Neurological/neuropsychiatric symptoms may be the only clinical manifestation of WD (Neurogenetics Group of the Neurology Branch of the Chinese Medical Association.2021)	I a	A
	Neurological and psychiatric symptoms of WD often appear later than hepatic symptoms(Neurogenetics Group of the Neurology Branch of the Chinese Medical Association.2021)	I b	B
	Psychiatric manifestations are depression, paranoia, hallucinations and delusions, irritability, loss of sexual inhibition, or decreased performance in school or at work(Ferenci et al. 2003,Litwin et al.2019)	I a	A
	Psychiatric symptoms may occur 2-3 years before the onset of neurological symptoms(Litwin et al.2019)	II b	A
	Behavioral and psychiatric symptoms (depression, personality changes, irritability, and incoherent behavior) are more common in patients with neurological involvement than in those with hepatic involvement(Chinese Medical Association, Hepatology Branch,2022)	I b	A
	Those with a predominantly neuropsychiatric presentation should be differentiated from Parkinson's disease or other causes of Parkinson's syndrome, various causes of dystonia, chorea, primary tremor, other causes of psychiatric abnormalities, and epilepsy(Ferenci et al.2003)	II b	B
Non-pharmacological treatment	Once patients are diagnosed with WD, a lifelong low-copper diet is required(Socha et al.2018,Ferenci et al.2003)	I a	B
	Severe neurological or psychiatric symptoms are not an indication for liver transplantation, as patients with irreversible neurological damage liver transplantation does not improve their symptoms and may even worsen neurological symptoms after surgery, therefore liver transplantation is not indicated for this group of patients(Ferenci et al.2003)	I a	B
	Liver transplantation is not recommended when neuropsychiatric symptoms are the predominant clinical phenotype (Litwin et al.2019)	I a	A
	Except for liver transplantation, all other treatment options should be lifelong and uninterrupted (Saroli et al.2012,Tampakia et al.2020)	I a	B

Category	Evidence content	Evidence level	Recommendation level
Drug treatment	Patients with WD with neuropsychiatric symptoms may be treated with zinc or chelating agents(Neurogenetics Group of the Neurology Branch of the Chinese Medical Association.2021)	I a	A
	Except for evidence of independent psychiatric conditions or recurrent psychiatric symptoms in WD, a gradual reduction in psychotropic medication should be considered after complete remission of symptoms(Medici et al.2007)	I b	B
	Monitoring of cognitive status is required when using psychotropic medications that can affect cognition(Medici et al. 2007)	II b	B
	Psychotropic medications should be considered independently of primary treatment for WD(Medici et al.2007)	II c	B
	25. Sodium dimercaptosuccinate is recommended for patients with WD who have neurological and psychiatric symptoms, as well as for patients with WD who cannot tolerate D-penicillamine or whose symptoms worsen with D-penicillamine(Socha et al.2018,Ferenci et al.2003)	II a	B
	26. Dimercaptosuccinic acid capsules are recommended for WD patients with mild to moderate liver damage and neuropsychiatric symptoms, especially if the patient is allergic to or intolerant to D-penicillamine(Medici et al.2007,Ferenci et al.2003)	II a	B
	27. Psychiatric symptoms of WD can be controlled by 5-hydroxytryptamine reuptake inhibitors or neuroleptics(Mulligan et al.2020)	II b	B
	Patients whose primary characteristic is neuropsychiatric symptoms should be initiated with zinc(Litwin et al.2019)	IV a	B
	29. Psychiatric medications with good safety and efficacy are recommended to be preferred for the treatment of psychiatric symptoms in patients with WD(Michael et al.2021)	I a	A
	30. The decision to initiate treatment for psychiatric disorders and the choice of medication should be made by a psychiatrist in conjunction with a WD specialist to avoid potentially hepatotoxic medications and treatments that may induce drug-related movement disorders(Michael et al.2021)	I c	B
	31. Given the high risk of exacerbation of neuropsychiatric symptoms after D-penicillamine treatment, it should be used with caution in patients with severe neurological symptoms(Chinese Medical Association, Hepatology Branch.2022)	II a	A
	32. Penicillamine needs to be increased slowly by 125-250 mg per week in adult patients with psychiatric symptoms(Shribman et al.2022)	I c	B
Health Education	Patients should avoid foods and water with high copper content during the 1st year of starting treatment (Saroli et al.2012,Michael et al.2021,Shribman et al.2022)	II a	B
	34. Routine monitoring indicators include serum copper, serum copper cyanide, liver biochemistry, international normalized ratio, liver function indicators, complete blood count, urine routine, and physical and neurological examinations at least twice a year (European Association for Study of Liver.2012,Nagra et al.2019,Ferenci et al.2003,Litwin et al.2019,Michael et al.2021,Tampakia et al.2020)	I c	B
	35. 24-h urine copper levels were measured at least once a year during drug therapy and 2 d after cessation of therapy. Measurement of non-copper blue protein bound serum copper may be another useful indicator of control therapy (European Association for Study of Liver.2012,Ferenci et al.2003,Michael et al.2021)	I c	B
	36. The Global Assessment Scale is a comprehensive, reliable, and validated scoring system for WD disease and can be used to assess the effectiveness of treatment during follow-up of WD patients with neuropsychiatric disorders(Neurogenetics Group of the Neurology Branch of the Chinese Medical Association.2021)	I b	B
	37. Ultrasound of the liver and spleen can be used to assess disease progression and monitor the effectiveness of medication and is recommended once every 3-6 months(Ferenci et al.2003)	I c	B
	38. Adherence can be checked by measuring 24-hour urinary copper excretion(Litwin et al.2019)	I c	B
	39. The choice of anti-copper medication may not be as important as ensuring adherence to lifelong treatment and regular treatment monitoring (Mulligan et al.2020)	IV a	B
	40. Patients with neuropsychiatric symptoms need to visit a specialist at least once a year for follow-up evaluation after starting treatment(Shribman et al.2022)	IV a	B
	41. When WD is suspected, immediate contact with a specialist center should be made(Shribman et al.2022)	I c	B

Figure 1 Flow chart of literature screening



DISCUSSION

Pre-diagnostic screening and evaluation of patients with hepatomegaly

Based on pertinent clinical symptoms and a variety of laboratory tests, hepatomegaly is screened for (Shribman et al. 2022). The target population, screening instruments, and screening indicators for mental disorders are all described in the evidence from Articles 1 to 7, respectively. Hepatomegaly mental condition continues to be misdiagnosed and underdiagnosed frequently; according to one study, the current prevalence of misdiagnosis and underdiagnosis for this disorder is as high as 49.3%. (Poujois et al. 2017,Laurencin et al. 2017). The majority of patients with hepatomegaly who appeared with mental issues were incorrectly classified as having other diseases due to the receiving physicians' lack of clinical experience or lack of attentiveness. Early diagnosis of hepatomegaly is crucial to the treatment and rehabilitation of the disease because a small percentage of patients with rapidly progressing or untreated disease develop severe liver and neuropsychiatric damage due to delayed optimal treatment, resulting in disability or even death at a later stage (Xu et al. 2014). When treating patients whose first clinical symptom is a mental disorder with extrapyramidal symptoms or other organ damage, doctors should actively pursue the patient's medical history, perform thorough neurological investigations, improve cranial MRI and corneal K-F ring examinations, and conduct detailed neurological investigations to lower the risk of underdiagnosis and misdiagnosis of the disease.A 4.08% prevalence of hepatomegaly in the progeny was found in the study by Dziezyc et al, which involved screening 1050 relatives of 760 patients with hepatomegaly. In a single gene line, the monogenic disease hepatomegaly can progress over numerous generations (Hahn 2014). Thus, thorough screening of patients'

parents, siblings, and children is required to quickly and accurately determine the presence and severity of hepatomegaly. The most often used tests include genetic testing, K-F rings, blood copper, 24 hour urine copper, and serum copper blue protein (Mulligan & Bronstein 2020). In-depth genetic testing can increase the identification rate because the majority of relatives of individuals with hepatomegaly do not exhibit symptoms of the condition. Even so, it is pricey and ineffective for doing a blind screening of applicants. On the other hand, copper cyanide testing is a relatively viable way of patient screening because it is straightforward, rapid, easy to do, minimally intrusive, and moderately priced. A considerable decrease in copper blue protein (100 mg/L) is nonetheless solid evidence for the diagnosis of hepatobiliary degeneration, despite the fact that standard copper blue protein screening for this condition has a specific false negative rate (Dziezyc et al. 2014, Li et al. 2019). Moreover, screening tests should be separated from organic brain conditions including Alzheimer's disease, Parkinson's disease, and Huntington's chorea on an individual basis. To achieve homogeneity and precision in screening, it is therefore necessary to develop additional standardized, uniform, and practicable screening protocols based on the summary of the evidence, to improve screening diagnosis, and to make clinical decisions by taking into account clinical scenarios and individual differences, analyzing facilitating and hindering factors, etc. Measures relevant to the assessment of mental disorders are summarized in the evidence from Articles 8 to 10. As managers and facilitators of patients' in-hospital life and health recovery, nursing staff should thoroughly assess patients' mental status and symptoms of other body systems and improve communication with patients and their families to help reduce the misdiagnosis rate of patients with hepatomegaly. Hepatomegaly with psychiatric disorders as the first symptom can easily be misdiagnosed as other organic brain diseases and miss the best time for treatment. This study offers medical practitioners a more thorough screening category for hepatomegaly symptoms, which will assist them in lowering the rate of hepatomegaly misdiagnosis and enhancing patients' quality of life and wellbeing by making decisions regarding many elements of clinical diagnosis.

Clinical presentation of patients with hepatomegaly at diagnosis

Hepatomegaly clinical symptoms related with psychiatric disorders are expressed in the evidence from Articles 11 to 16. Hepatomegaly typically develops slowly in most people, with psychiatric issues being the initial sign in about 20% of instances (Litwin et al. 2019). Yet, because to a lack of information and comprehension of hepatomegaly, the majority of symptoms are only recognized when they coexist with neurological or hepatic problems. The most prevalent sudden emotional instability, depression, and cognitive impairment are psychiatric symptoms that are non-specific, can arise at any stage of the illness course, and are often mistaken for psychiatric disorders (Beiraghi et al. 2018).Patients with hepatomegaly tend to experience hallucinatory delusions less frequently than other psychiatric symptoms. According to prior studies of psychiatric diseases brought on by hepatomegaly around the world, clinical psychiatric symptoms in hepatomegaly patients tend to be largely emotion-related, like depression or crying uncontrollably, with a few cases of hallucinatory delusions (Roberts & Schilsky 2008, Elyasi 2017). Mental retardation is more obvious when the condition is more advanced. This study suggests that medical professionals should be particularly aware of mental disorders in clinical practice and should carefully screen for them in the context of the patient's specific clinical symptoms and pertinent laboratory tests in order to decrease the likelihood of misdiagnosis in patients with WD. The neurological genetic condition hepatomegaly, which is most frequently diagnosed in teens, is typically well-treated. Therefore, early identification and therapy are crucial for a successful copper-repellent response since their outcomes are directly correlated. This study offers evidence-based recommendations based on various recipient populations, suggesting that patients should increase their understanding of the disease and its various manifestations, family members should monitor pertinent indicators to stop the disease before it starts, clinical staff should strengthen the disease's promotion and research and development, and summarize more trustworthy screening and treatment methods. To improve the social welfare system, increase funding for rare diseases, address the issue of patient and family poverty brought on by the disease, and truly achieve early detection, early diagnosis, early treatment, and lifelong treatment for patients, the government should collaborate with social agencies. The study also discovered that copper metabolism was maintained at an average level, speech confusion and mobility problems in the later stages were reduced, readmission rates were reduced to a greater extent, the quality of life of hepatomegaly was improved, and better treatment and rehabilitation in the later stages were achieved by providing scientific and theoretical guidance to hepatomegaly through the "three early stages." Rehabilitation and treatment were improved.

Interventions for patients with hepatomegaly at diagnosis

The evidence for non-pharmacological therapies for hepatomegaly is compiled from publications 17 to 20. After hepatomegaly is detected, patients must follow a lifelong low-copper diet, and treatment should not be discontinued for life. The main goal of hepatomegaly treatment is to restore normal copper homeostasis by balancing copper absorption and excretion (Ying et al. 2019). Additionally, it has been established that severe psychiatric symptoms do not indicate liver transplantation despite the fact that liver transplantation is the most effective treatment for hepatomegaly due to the patient's irreversible psychiatric disorder and the possibility of worsening organic symptoms following surgery (Poujois & Woimant 2018a).

Evidence from Articles 21 to 32 summarizes, in terms of indications, side effects, and particular mechanisms, the issues connected to the use of medications for psychiatric diseases. Treatment for hepatomegaly aims to create a copper balance that is net negative. Body copper stabilization in patients with copper excess can be accomplished by boosting excretion by chelation therapy, while lowering copper absorption via zinc and reducing dietary consumption (Jacquelet et al. 2018,Tampakia et al. 2020).

The effectiveness of several anti-copper medications varies greatly: For hepatomegaly with mild to moderate liver damage and neuropsychiatric symptoms, sodium dimercaptopropionate and dimercaptosuccinic acid capsules are advised, especially if the patient is allergic to or intolerant to D-penicillamine; hepatomegaly with neuropsychiatric symptoms can be treated with zinc or chelating agents, which act as chelating agents by binding to copper, inducing copper excretion from the urine and promoting copper Because pharmacological mechanisms, side effects, and efficacy differ, it is important to monitor effects and cognitive status when using psychiatric medications and to stop taking them as soon as possible. It is advised that patients start customized treatment early and continue to lifelong treatment for hepatomegaly because persons with the condition respond to medicine in a variety of ways. Patients' knowledge of copper and their capacity to resist it have grown as a result of the advent of internet medicine and chronic disease management models. A personalized anti-copper drug management program can help standardize anti-copper, improve patients' capacity for self-management, foster a positive outlook on life, instill confidence in their futures, and help them better understand their own value.

Health education for patients with hepatomegaly after diagnosis

The researchers summarized the evidence and discovered that some papers employed health education as a subtly effective technique to assist patients in understanding the dangers, symptoms, and preventative measures connected to hepatomegaly. Health education is referred to as a crucial component of clinical care in Evidences 33 to 41. Because to the unique characteristics of this organic brain disease, individuals with hepatomegaly have a lack of self-management skills. This causes a huge load on patients and their families and negatively impacts both the quality of life of patients and caregivers (Huang et al.2022). According to this study, health education regarding the fundamentals of the disease, dietary guidelines, exercise routines, and health care should all be focused while treating disease-related symptoms. One of the main causes of poor treatment compliance and high readmission rates is patients' ignorance of their diseases. In order to improve clinical outcomes and the effectiveness of subsequent rehabilitation, it is crucial to enhance patient health education while treating disease-related symptoms. This includes providing patients with targeted information about basic disease knowledge, diet, exercise, and health care, as well as responding to national policy that encourages continuity of care and extends medical services to rural areas and communities. To improve patients' compliance behavior compliance, promote patients' physical and psychological recovery, and increase patients' confidence in treating diseases, it is also important to offer patients and their families with regular psychological support. Regular treatment monitoring is more successful than single-stage anti-copper therapy for patients with hepatomegaly, and compliance is a crucial component in prognosis (Zhang & Hu 2013). Numerous studies have also recommended that patients be followed up with at least twice a year in order to monitor symptoms, improve their condition, reduce side effects of treatment, and have routine check-ups in order to prevent the rapid deterioration of symptoms caused by noncompliance with prescribed medication. Patients and their families will receive long-term, recurrent, and extensive education so that they are properly informed about the disease and the medical controls needed to establish a stable condition (Poujois et al.2018b). Good health education can help patients better their level of awareness, self-care, and self-management by assisting them in learning about the traits of the condition and the implications of its treatment. Health education can increase patients' understanding of their condition and

compliance with prescribed behaviors, lowering the rate of stage readmission for hepatomegaly patients, conserving medical resources, and significantly accelerating their recovery.

CONCLUSIONS

This study offers a pertinent basis for early screening, quasi-assessment, stable treatment, and appropriate health education for the treatment of disease in patients with hepatomegaly by clinical staff. It also summarizes the evidence for early screening, quasi-assessment, stable treatment, and the management of psychiatric disorders in patients with hepatomegaly. It improves the full spectrum of therapy for patients with hepatomegaly. The included material varies in terms of views, conceptions, and attitudes about hepatomegaly due to geographic and cultural variances. It is advised that while using pertinent clinical evidence, the particular resource environment and elements that help and impede the use of proof should be assessed. Then, evidence should be chosen as necessary. The best available data must be applied to clinical practice in order to create customized intervention plans that assist patients more significantly.

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