CLDF

Chronic Liver Disease Foundation

Unparalleled expertise, unprecedented access

2021 | Year in Review

Letter from the President

As of February 2022, the Chronic Liver Disease Foundation (CLDF) marked **20 years** as a not-for-profit educational organization, led by an all-volunteer board of trustees. Since its inception, CLDF has led the field by providing exceptional programming in liver disease.

2021 was highlighted by the inauguration of the first Liver Connect Conference engaging over 230 healthcare providers in a live setting and hundreds more joining through live meeting broadcast. The purpose of this unique annual conference is to connect clinical evidence from scientific discovery to the clinical practices of gastroenterologists, hepatologists, advanced practice providers, primary care physicians, endocrinologists and other providers involved in the care of patients with liver disease.

This 2-day conference in 2021 featured renowned disease experts from across the country, including a noble laureate, who delivered state-of-the-art presentations. This was a unique opportunity for all to convene after a year of exclusively virtual meetings due to Covid-19.

As an organization, CLDF has continued to provide innovative education to all stakeholders. The Expert Perspective live broadcasts and enduring webcasts from CLDF have offered providers across the country an opportunity to learn from highly regarded specialists in their field. The successful collaboration with Project ECHO and recovery institutions to educate and screen for Hepatitis C continues to be first in class.

The commitment and professionalism of our expert clinical advisors, program staff, CME accredited providers, and network of collaborators have been key drivers of another successful year in delivering state-of-the-art programming.

As we move into 2022, the Chronic Liver Disease Foundation remains committed to patients with liver disease and to the field of hepatology by continuing to deliver cutting-edge, highly meaningful educational programs. We greatly appreciate the commitment and support from our advisors and all partners.

Sincerely,

Zobair M. Younossi, MD, MPH
President and Chairman, CLDF Board of Trustees

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2021 Programs

Alcohol Liver Disease
Cholestatic Liver Disease
Cirrhosis
Hepatorenal Syndrome
HCC
NAFLD/NASH
Pediatric Liver Disease
Viral Hepatitis
Wilson Disease

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INAUGURAL LIVER CONNECT

APRIL 15-17, 2021

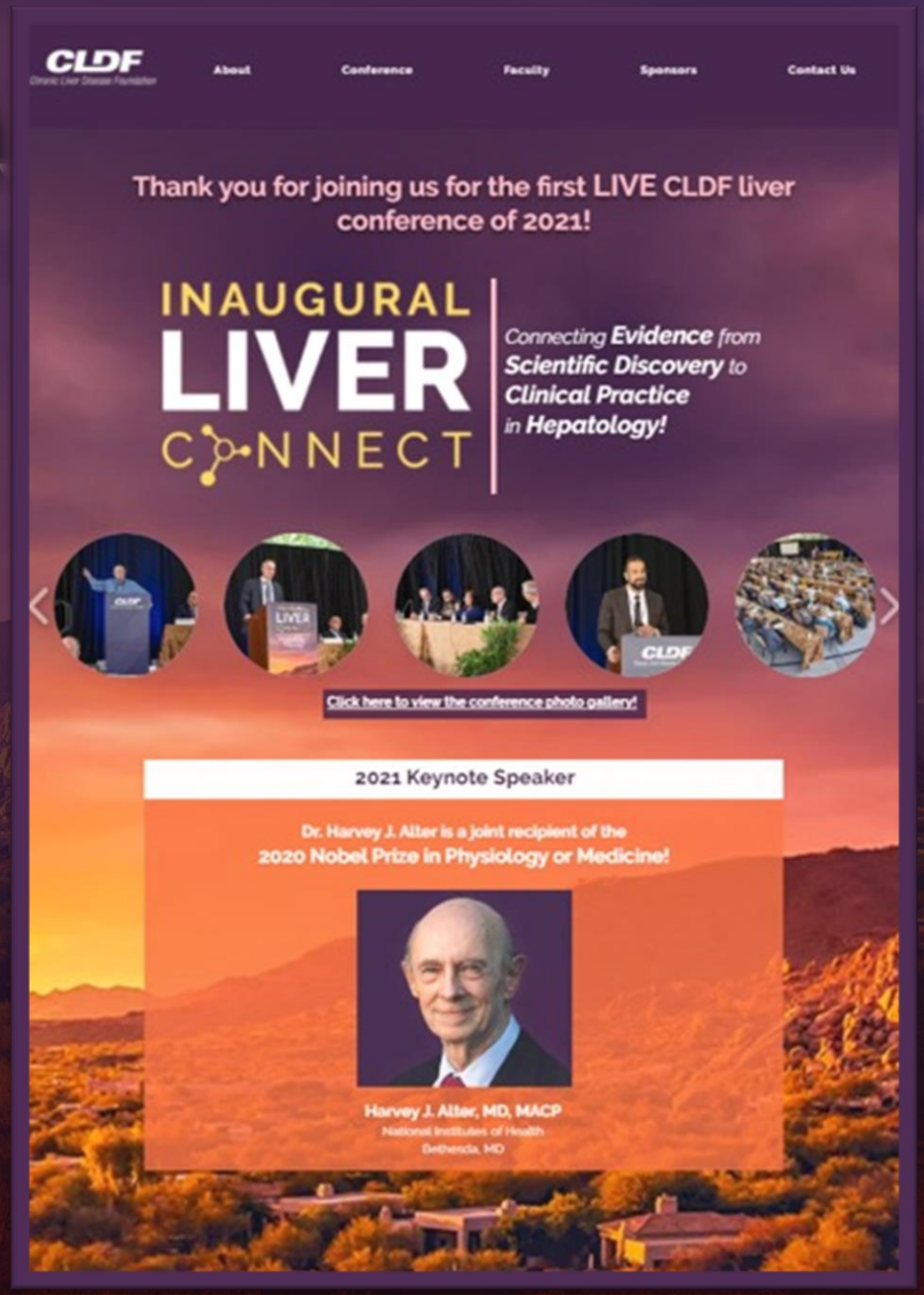
231 *live participants*

421 *virtual*

2 *day meeting*

8.5 *Credit Hours*

In addition to the conference, the CLDF hosted a **Global NASH Leadership Summit** and **Committee Meetings**.



CLDF continues on its tradition of offering the Xpert Perspectives education series. This on-demand presentation covers the latest research updates and expert opinions on diagnosis and treatment advances PFIC and ALGS.

Educated over 200 participants

TRIPLE E FOR HCV

TREATMENT EXPANSION IN HIGH-RISK COMMUNITIES

ENGAGEMENT, EDUCATION AND ERADICATION OF HCV

In 2021, the CLDF continued to join the global efforts in eliminating HCV by continuing the education and screening program: **Triple E for HCV**. This program focused on educating, screening, and linkage to care for healthcare providers and patients in addiction/substance abuse facilities.

2021

- **43** screening events
- **921** persons screened
- **283 (30.7%)** Antibody +
- **260 (91.8%)** Blood Draw Completed
- **163 (62.6%)** HCV RNA +
- **669** Staff Educated

Educating
Patients & Staff

Screening
for HCV

Link to
Hepatitis
Management Experts

Counseling
Patients

Overall

- **128** screening events
- **4,650** persons screened
- **1,812 (39.0%)** Antibody +
- **1,453 (80.0%)** Blood Draw Completed
- **952 (65.5%)** HCV RNA +
- **1,739** Staff Educated

Prisoner Health is Community Health

The New Mexico Peer Education Project

The CLDF and The New Mexico Peer Education Project (NMPEP), continued collaborating with Project ECHO at the University of New Mexico Health Sciences Center and the New Mexico Corrections Department, leveraging the ECHO Model to make a powerful and lasting intervention in prison community health.

The *HALT HCC: A National Live Broadcast and Archive*, is a unique experience that provides education on the latest emerging data for the management and treatment of HCC. The HALT HCC broadcast and archived versions were promoted to a national audience of specialists and allied healthcare professionals.

Educated over **300+** **live and** **550+** on-demand

Clinical advances in the diagnosis and management of patients with cirrhosis of the liver have advanced rapidly over the past decade. As new advances in diagnostic and treatment approaches are introduced, clinicians continue to participate in the CLDF Hot Topics programs.

Educated over 160 participants

HRS Summit

Key advisors gathered for a thorough, updated review of the disease state, medical management in the US, and current data.

Andrew Allegretti, MD	Steven Flamm, MD	Chirag Parikh, MD	George Therapondos, MD
Justin Belcher, MD	Todd Frederick, MD	Rajender Reddy, MD	James Trotter, MD
David Bernstein, MD	Yuri Genyk, MD	Joykumar Patel, MD	Eugenia Tsai, MD
Terry Box, MD	Stevan Gonzalez, MD	Kevin Regner, MD	Hugo Vargas, MD
Kimberly Brown, MD	Aftab Karim, MD	Sammy Saab, MD	Juan Carlos Velez, MD
Robert Brown, MD	Marcelo Kugelmas, MD	Obaid Shaikh, MD	Hani Wadei, MD
Andres Cardenas, MD	Kevin Moore, MD	Douglas Simonetto, MD	Mark Wong, MD

After the Summit, the CLDF collected 86 signatures to be included in a letter to the FDA requesting approval of Terlipressin for HRS-AKI.

A manuscript titled **The Current Management of Hepatorenal Syndrome-Acute Kidney Injury in the United States and the Need for Additional Treatment Options** was published in *Liver Transplantation* in April 2021.

THE CHRONIC LIVER DISEASE FOUNDATION PRESENTS:

NEW ADVANCES IN NASH DIAGNOSTICS AND PROGNOSTICS

The *New Advances in NASH Diagnostics and Prognostics* symposia series delivered focused, educational updates highlighting clinically relevant advances in the management of obesity, NAFLD and NASH. The educational initiative includes seven hybrid regional conferences featuring didactic and clinical case discussions on the management of NASH.

To date, we have educated 380 participants

ACCREDITED BY

UNIVERSITY OF Cincinnati

SUPPORTED BY AN EDUCATIONAL GRANT FROM SIEMENS HEALTHCARE DIAGNOSTICS, INC.

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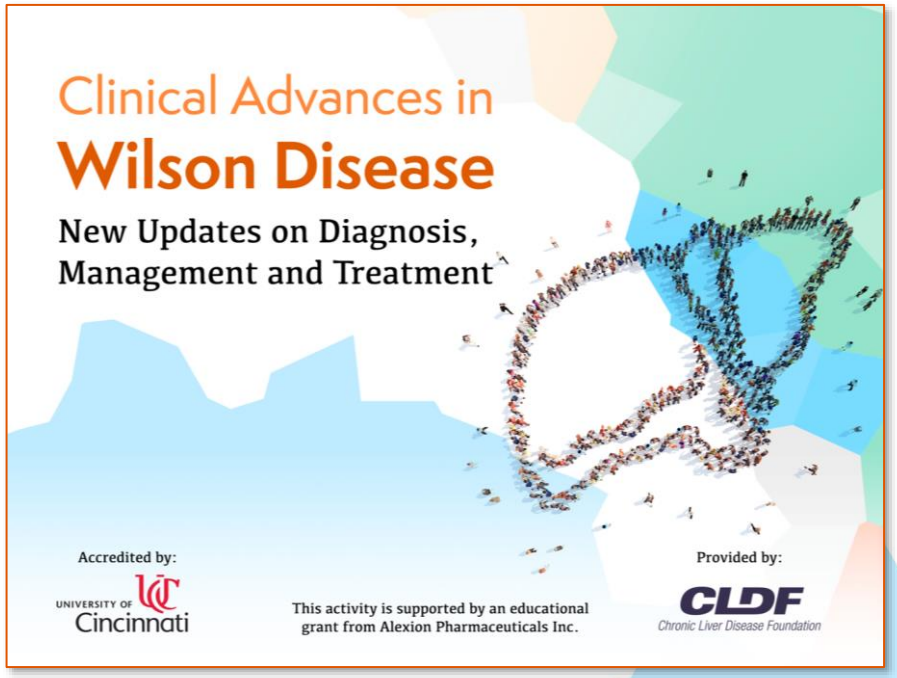
CLDF Wilson Disease Education



Program Agenda

Clinical Advances in Wilson Disease

- Welcome and Introduction
- Pathophysiology and Epidemiology
- Clinical Presentation and Diagnosis including AASLD Guidelines Recommended Approach
- Current treatment options for WD including a case study
- Data on Novel Therapies Under Investigation for the Treatment of WD
- Discussion and Q&A
- Adjournment

Educational Objectives

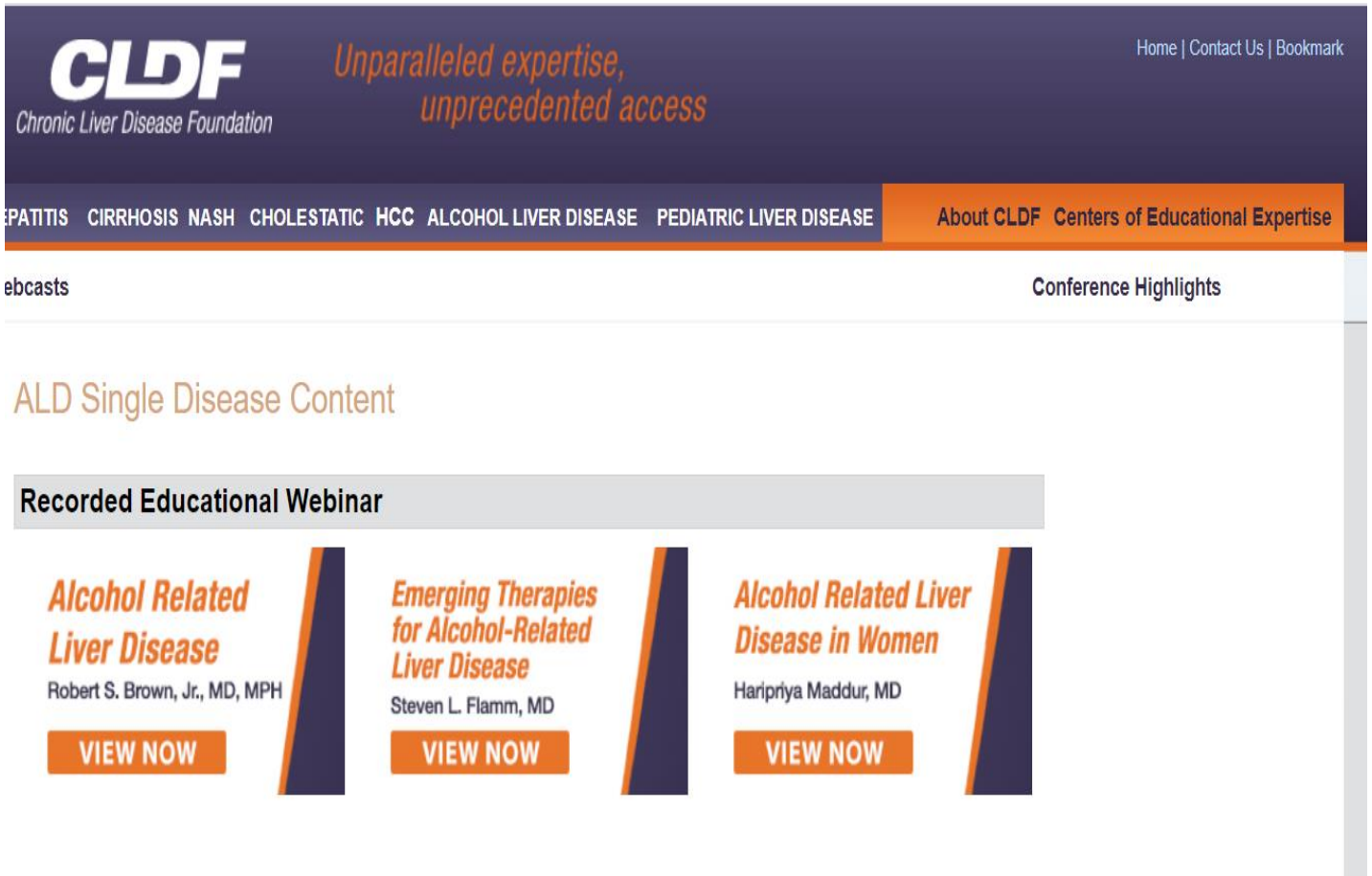
Upon completion of this activity, participants should be able to:

- Describe the importance of and recommend approaches for the early identification of Wilson disease
- Demonstrate strategies to incorporate diagnostic and management recommendations into clinical practice
- Discuss and review data on established and investigational therapies for Wilson disease

Live and Virtual Meeting Series

Webcast posted on CLDF site

Alcohol Liver Disease Webcasts



As the need for education rises regarding alcohol-related liver disease, the CLDF formed a committee dedicated to ALD, and developed education disseminated through the CLDF website.

Publications

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CLDF AASLD Abstract Review

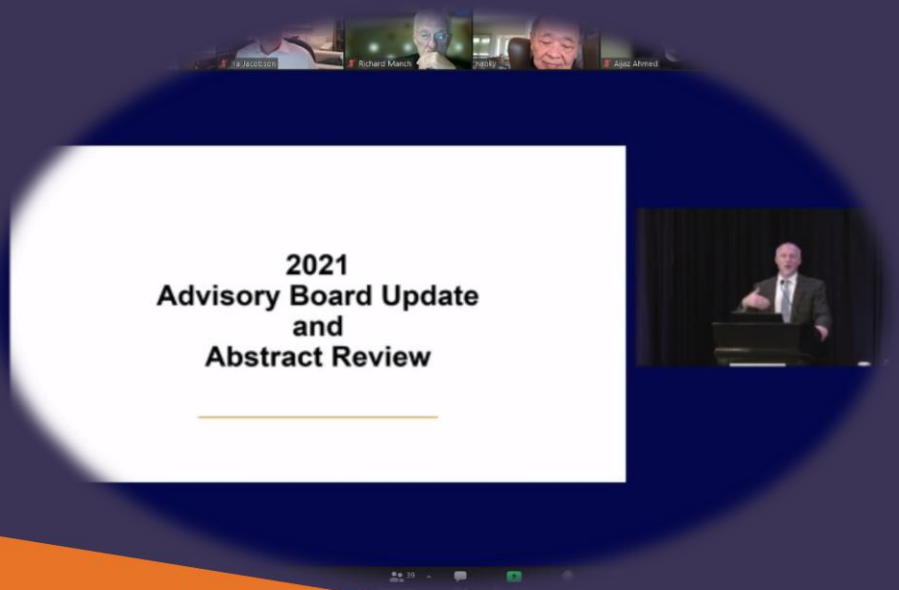
140 Abstracts Reviewed on 8 topics:

NAFLD/NASH *Cholestatic Liver Disease* *HCV* *HBV/HDV*

HCC and Liver Transplant *Complications of Cirrhosis* *Pediatric Liver Disease*

75 Independent Reviewers

63 Virtual and Live Attendees



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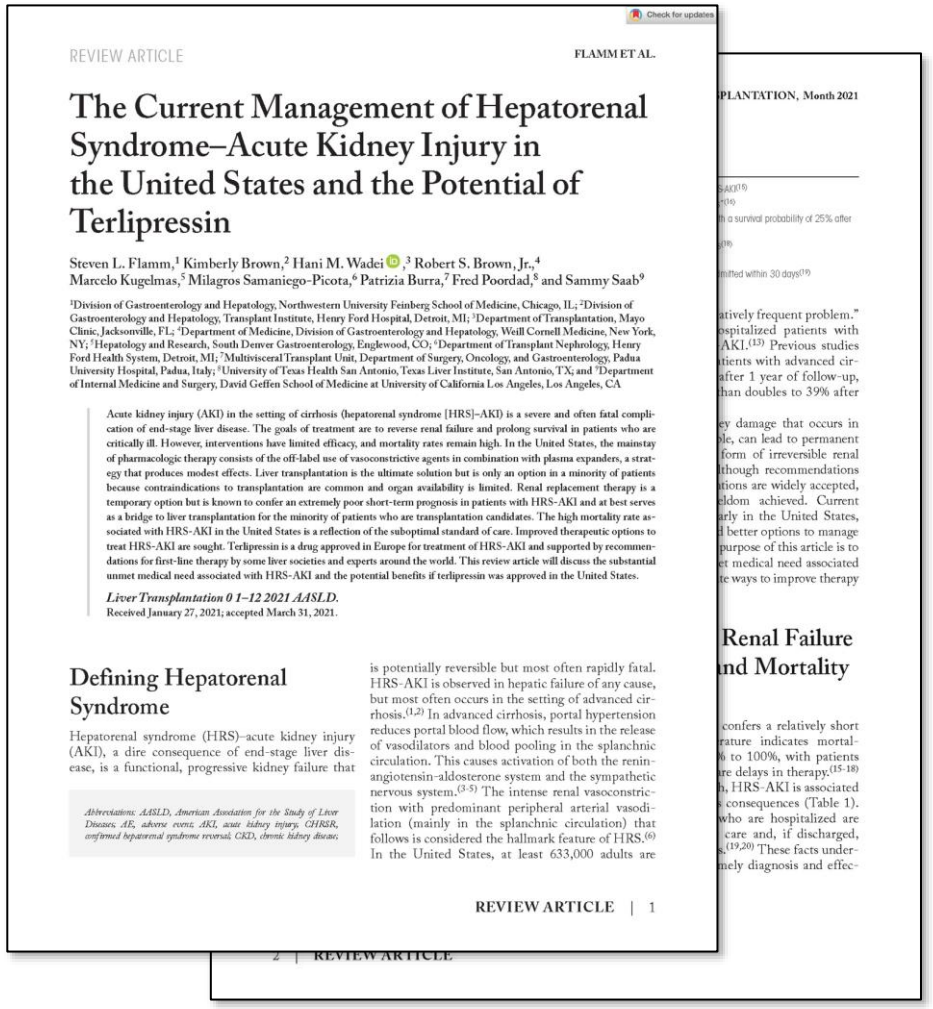
Article published in *Liver Transplantation* April 2021

PUBLISHED ONLINE APRIL 2021 *Liver Transplantation*

The Current Management of Hepatorenal Syndrome–Acute Kidney Injury in the United States and the Potential of Terlipressin

VIEW NOW



REVIEW ARTICLE FLAMM ET AL.

The Current Management of Hepatorenal Syndrome–Acute Kidney Injury in the United States and the Potential of Terlipressin

Steven L. Flamm,[1] Kimberly Brown,[2] Hani M. Wadei,[3] Robert S. Brown, Jr.,[4] Marcelo Kugelmas,[5] Milagros Samaniego-Picota,[6] Patrizia Burra,[7] Fred Poordad,[8] and Sammy Saab[9]

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Acute kidney injury (AKI) in the setting of cirrhosis (hepatorenal syndrome [HRS]–AKI) is a severe and often fatal complication of end-stage liver disease. The goals of treatment are to reverse renal failure and prolong survival in patients who are critically ill. However, interventions have limited efficacy, and mortality rates remain high. In the United States, the mainstay of pharmacologic therapy consists of the off-label use of vasoconstrictive agents in combination with plasma expanders, a strategy that produces modest effects. Liver transplantation is the ultimate solution but is only an option in a minority of patients because contraindications to transplantation are common and organ availability is limited. Renal replacement therapy is a temporary option but is known to confer an extremely poor short-term prognosis in patients with HRS-AKI and at best serves as a bridge to liver transplantation for the minority of patients who are transplantation candidates. The high mortality rate associated with HRS-AKI in the United States is a reflection of the suboptimal standard of care. Improved therapeutic options to treat HRS-AKI are sought. Terlipressin is a drug approved in Europe for treatment of HRS-AKI and supported by recommendations for first-line therapy by some liver societies and experts around the world. This review article will discuss the substantial unmet medical need associated with HRS-AKI and the potential benefits if terlipressin was approved in the United States.

Liver Transplantation 0 1–12 2021 AASLD.
Received January 27, 2021; accepted March 31, 2021.

Defining Hepatorenal Syndrome

Hepatorenal syndrome (HRS)–acute kidney injury (AKI), a dire consequence of end-stage liver disease, is a functional, progressive kidney failure that is potentially reversible but most often rapidly fatal. HRS-AKI is observed in hepatic failure of any cause, but most often occurs in the setting of advanced cirrhosis.[1,2] In advanced cirrhosis, portal hypertension reduces portal blood flow, which results in the release of vasodilators and blood pooling in the splanchnic circulation. This causes activation of both the renin-angiotensin-aldosterone system and the sympathetic nervous system.[3-5] The intense renal vasoconstriction with predominant peripheral arterial vasodilation (mainly in the splanchnic circulation) that follows is considered the hallmark feature of HRS.[6] In the United States, at least 633,000 adults are

Abbreviations: AASLD, American Association for the Study of Liver Diseases; AE, adverse event; AKI, acute kidney injury; CHRSR, confirmed hepatorenal syndrome reversal; CKD, chronic kidney disease;

PBC Patient Journey Abstract Paper presented at ACG in October 2021

PBC PATIENT JOURNEY
A PILOT STUDY PROGRAM

Gaps in the Patient Journey Through the Diagnosis and Management of Primary Biliary Cholangitis

KIMBERLY BROWN, MD[1,2]; KRIS KOWDLEY, MD[2,3]; APURVA A. MODI, MD, MS, MHSc[2,4]
[1]Henry Ford Hospital Transplant Institute, Detroit, MI; [2]Chronic Liver Disease Foundation, Clark, NJ; [3]Liver Institute Northwest, Seattle, WA; [4]Baylor All Saints Medical Center, Fort Worth, TX

Background

- Primary biliary cirrhosis/cholangitis (PBC) is a chronic, inflammatory, autoimmune disease that primarily targets the cholangiocytes of the interlobular hepatic bile ducts and is associated with multiple systemic conditions such as Sicca Syndrome, thyroid disease, Raynaud's phenomenon and scleroderma.[1]
- Without treatment, PBC may progress to cirrhosis and liver failure and is frequently associated with impaired quality of life for patients.
- Systemic complaints such as fatigue, cognitive symptoms, social and emotional dysfunction, sleep disturbance, and depression and pruritus require long term follow-up and management[2]
- Treatment of PBC is directed at both the underlying disease and its complications[3]
- Ursodeoxycholic acid (UDCA) is used as a first-line treatment to slow disease progression[3]
- Obeticholic acid (OCA) is FDA-approved for the treatment of PBC in combination with UDCA in patients with an inadequate response to UDCA, or as a monotherapy in patients unable to tolerate UDCA[3]
- Up to 40% of patients don't respond (clinically, biochemically and/or histologically) to UDCA[3]
- The Chronic Liver Disease Foundation (CLDF) is a nonprofit educational organization comprised of hepatologists and dedicated to increasing awareness of the effects of chronic liver disease in the US

Aim

- Review the patient journey in patients diagnosed with PBC
- Gain a better understanding of the current diagnosis and treatment approaches for PBC by hepatologists, gastroenterologists and primary care providers
- Identify potential gaps in both the diagnosis and treatment of PBC amongst providers
- Variations exist between community and academic sites in the process of diagnosis and care of PBC; this can impact patient outcomes

Methods

- Patients diagnosed with PBC from 7 institutions were included
- Participating providers were Gastroenterologists or Hepatologists from both community and academic practices
- The diagnosis of PBC was based on current AASLD criteria requiring 2 of the following criteria to be met:
  - Biochemical evidence of cholestasis based on ALP elevation
  - Presence of AMA
  - Histologic evidence of nonsuppurative destructive cholangitis and destruction of interlobular bile ducts
- Inclusion criteria included
  - Age ≥ 18
  - Past or current treatment with UDCA
  - Ability to read and understand English
  - ≥ 4 documented PBC laboratory assessments within 3 years or ≥ 5 office visits
- Data was collected and entered both prospectively and by retrospective chart review into RedCap, a web based application utilized to capture and analyze data
- Patients with documented additional diagnoses including HCV, HBV, NAFLD, NASH may be included if diagnostic criteria for PBC was met

Results

Diagnosis and Staging

- 68% of patients were diagnosed previously by another provider (gastroenterologist (64%), hepatologist (21%), internal medicine (3%), unknown (10%)) and referred to or followed by the research respondent
- 32% of HCP research respondents made the initial PBC diagnosis in their patients, and of those patients:
  - 47% had unconfirmed stage of disease
  - Of the 53% with a confirmed stage of disease, most were diagnosed with stage 1 (22%), followed by stages 2 and 3 (both 11%), then stage 4 (8%)
- 70% of patients underwent liver biopsy at the time of diagnosis with the majority showing Stage 1 or 2 disease (Figure 3)
- 30% of patients were diagnosed without a biopsy (Figure 4)
  - Laboratory tests including ALP, SGPT/ALT, SGOT/AST and bilirubin levels were most commonly used
  - Fibroscan was infrequently used at or following the diagnosis with fibroscan assessment used in only 5% of patients over the study period

Symptoms

- The most common current symptoms were fatigue (32%) and pruritus (30%) (Figure 5). With regard to fatigue, the majority of patients experienced mild fatigue (55%), followed by moderate (28%), then severe (17%). With regard to pruritis, most cases were mild (64%), with 36% experiencing moderate pruritis. No severe cases of pruritis were reported.

Pruritis Symptom Management

- Antihistamines (61%) and cholestyramine (29%) were primarily used to manage patients' pruritus symptoms (Figure 6)
- Vitamin D3 (10%), nutritional supplements (7%) and antidepressants (7%), followed by various other approaches including pain medication and antihistamines, were most commonly used to manage fatigue
- Artificial tears (44%) and nutritional supplements (13%) were used to manage Sicca Complex

Frequency of Lab Testing

- The majority of HCPs (79%) indicate their PBC patients visit their office 2+ times per year
- The majority of HCPs (54%) conduct lab tests on an "as needed" basis to monitor patients' PBC progression; 41% of HCPs indicate they conduct lab tests 2+ times per year.
  - Patient records indicate only 50% of patients actually had lab tests conducted 2 or more times per year

Laboratory Monitoring

- The mean time between presentation labs to most recent labs was ~4 years
- Overall (Table 2), when comparing presentation labs to most recent labs, the majority of PBC patients (75%) had a decrease in ALP and more than a third (39%) had a decrease in bilirubin levels
- When comparing ALP presentation labs to most recent labs, there was a significant increase in the number of patients falling within the normal range while those uncontrolled dropped to 25%
- While less of a shift than ALP, most recent bilirubin labs show 85% of PBC patients within normal range

PBC Treatment

- Overall, 93% of patients currently receive or plan to receive UDCA, while 19% currently receive or plan to receive OCA
- 47% of patients' recent lab results meet OCA criteria (ALP>160):
  - Of these, only 32% currently receive/plan to receive OCA, while 94% remain on UDCA
- Those who chose not to treat with OCA indicate patients:
  - Are well controlled/stable with UDCA (54%)
  - Do not need adjunctive therapy (13%)
  - Had contraindications to OCA use (eg, pruritis, cirrhotic disease, 15%)
  - Were intolerant to OCA (AP did not drop by 15%, OCA use demonstrated no effect, decompensation, itching; 15%)

Laboratory Response to Treatment

- Over the study period, ALP decreased in 75% of patients with 45% falling into the normal range
- 77% of patients on OCA (n=22) had a decrease of ALP on treatment as compared with 60% of patients on UDCA alone (Figure 7)

Table 1. Patient Demographics

PBC Stage of Disease	Frequency of Labs
Gender	87% female; 13% male
Age	Average age was 63 years old
Level of education	60% obtained a high school degree; 19% received a bachelor's degree; an additional 19% received an advanced degree
Working or retired	38% had full or part time employment; 54% retired

Figure 1. Family History

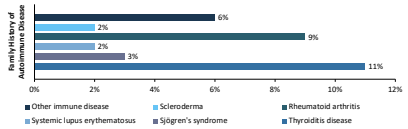


Figure 2. Specialist Making PBC Diagnosis

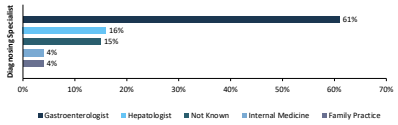


Figure 3. Stage of Disease – Initial Biopsy

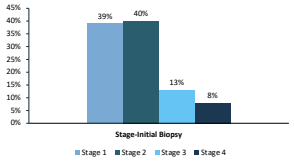


Figure 4. Diagnostic Tests Used for Diagnosis and Staging

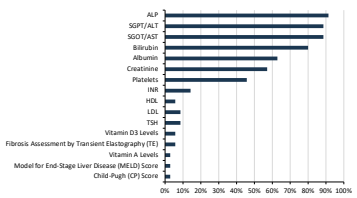


Figure 5. Current Symptoms

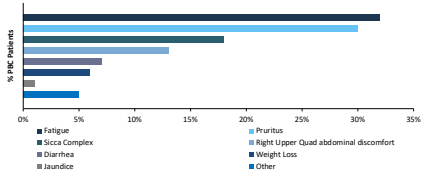
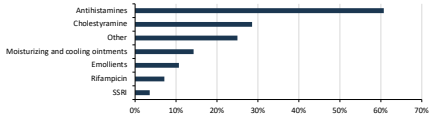


Figure 6. Pruritus Symptom Management

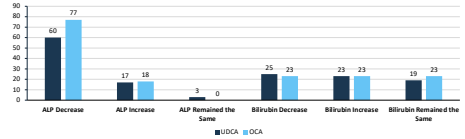


*Other= gabapentin, colestipol, HydrOCYzine HCl, Prednisone, Ursodiol

Table 2. Presentation Labs Compared to Most Recent Labs

Laboratory Test		Presentation Lab	Most Recent Lab	% Increase	% Decrease	% Same
ALP	Records	n = 95	n = 105	For comparison, n = 91		
	Normal 44-147	24%	45%	22%	75%	3%
	1.67 x ULN	29%	30%			
	Uncontrolled	46%	25%			
Bilirubin	Records	n = 79	n = 106	For comparison, n = 77		
	normal 0.1 - 1 mg/dL	81%	85%	34%	39%	27%
	>1mg/dL	19%	15%			

Figure 7. Changes in Laboratory Results Based on UDCA or OCA Use



Conclusions

- There are significant gaps between HCP perception and reported patient chart data regarding management and followup of patients with PBC
- The majority of patients showed improvement in biochemical parameters with treatment over time
- Significant gaps were seen in all aspects of PBC management including diagnosis, staging and treatment followup of patients with PBC in this study
- Institution of planned educational efforts toward PBC providers around current published guidelines for diagnosis, staging and medical management are likely necessary to close these gaps

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Abbreviations

AASLD, American Association for the Study of Liver Diseases; ALP, alkaline phosphatase; AMA, antimitochondrial antibody; HBV, hepatitis B virus; HCP, healthcare provider; HCV, hepatitis C virus; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase

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