REVIEW

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Progress and Perspectives in Overlapping Primary Biliary Cholangitis and Autoimmune Hepatitis: A Comprehensive Review

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ABSTRACT

Overlapping primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH) represents a distinctive autoimmune phenotype characterized by concurrent cholestatic and hepatocellular damage, culminating in a more aggressive disease course if not recognized. This review synthesizes the existing evidence concerning epidemiology, pathophysiology, and diagnostic criteria, with particular emphasis on histopathology, serological markers, and established scoring systems, including the Paris criteria and the International Autoimmune Hepatitis Group (IAIHG) scoring scheme. We highlight the clinical relevance of combined therapies, typically comprising ursodeoxycholic acid and immunosuppressants, in effectively controlling both components of the disorder and halting fibrosis progression. Additionally, we discuss emerging data regarding second-line agents such as obeticholic acid and innovative immunomodulatory approaches aimed at refining patient outcomes. Special attention is dedicated to pediatric and pregnant populations, in whom disease manifestation and therapeutic responses may differ. Ongoing evaluations of noninvasive biomarkers and imaging modalities, including transient elastography, promise improved monitoring and individualized management strategies. Notably, relevant outcome measures, including quality of life and the burden of pruritus, are paramount for comprehensive patient care. Collectively, these advances hold promise for improved long-term patient survival by enabling more precise diagnostic pathways, targeted therapeutic regimens, and closer surveillance.

Key words: primary biliary cholangitis – autoimmune hepatitis – overlap syndrome – immunopathology – prognosis – ursodeoxycholic acid – immunosuppression.

Abbreviations: AIH: autoimmune hepatitis; ANA: anti-nuclear antibody; anti-LKM-1: anti-liver kidney microsomal type 1; anti-SLA: anti SLA: soluble liver antigen; CTLA4: cytotoxic T-lymphocyte associated protein 4; HLA: human leukocyte antigen; IAIHG: International Autoimmune Hepatitis Group; IgG: immunoglobulin G; IL: interleukin; IFN-γ: interferon-gamma; PBC: primary biliary cholangitis; PDC-E2: pyruvate dehydrogenase complex E2 subunit; SMA: anti-smooth muscle antibody; SNP: single-nucleotide polymorphism; TNF: tumor necrosis factor; Treg: regulatory T cells; UDCA: ursodeoxycholic acid.

INTRODUCTION

Autoimmune liver diseases comprise a heterogeneous group of disorders that develop from a complex interplay between genetic predisposition and environmental triggers, leading to aberrant immune responses against hepatic structures [1]. Primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH) stand out as two prototypical conditions within this category, each exhibiting distinct clinical, serological, and histopathological hallmarks. PBC is primarily characterized by chronic, nonsuppurative destructive cholangitis of small intrahepatic bile ducts, which leads to cholestasis, biliary fibrosis, and eventual cirrhosis if untreated [2, 3]. On the other hand, AIH presents with predominantly hepatocellular inflammation, marked interface hepatitis, high immunoglobulin G (IgG) levels, and characteristic autoantibodies such as anti-nuclear antibody (ANA), anti-smooth muscle antibody (SMA), or anti-liver kidney microsomal type 1 (anti-LKM-1) [4].

While these entities were once considered mutually exclusive, clinical overlaps, commonly referred to as "overlap syndromes", are increasingly recognized [5]. Overlapping PBC-AIH is the most frequently encountered combination, though other overlaps (e.g., primary sclerosing cholangitis-

AIH) have also been described [6]. Overlap syndromes may be suggested by persistent cholestatic enzyme elevations in patients diagnosed with AIH, or alternatively by prominent hepatocellular damage in patients diagnosed with PBC [7]. Recognizing this overlap state is critically important due to its potential for an accelerated course, leading to earlier fibrosis, cirrhosis, and a diminished response to conventional monotherapy if not adequately treated [8, 9].

In the past two decades, growing awareness of overlapping PBC-AIH has led to more rigorous attempts to standardize its diagnosis and treatment [10]. The International Autoimmune Hepatitis Group (IAIHG) scoring system and the Paris criteria are widely utilized frameworks for identifying overlap, but variations in clinical presentation can render strict application of these criteria challenging [11]. The complexity arises from multiple levels: serological ambiguity (e.g., concurrent presence of anti-mitochondrial antibody and ANA/SMA) [12], histopathological diversity (i.e., mixed cholangitis and interface hepatitis) [13], and a dynamic disease course that may evolve over time [9].

In this comprehensive review, we provide an updated synthesis of the epidemiology and pathophysiology of overlapping PBC-AIH [14], elucidate current diagnostic strategies [3], and examine both established and emerging therapeutic modalities [15]. Special populations, such as pediatric patients and pregnant women, are also addressed given that their physiological differences may alter disease presentation and treatment. We conclude by highlighting ongoing challenges and future directions for research, emphasizing the promise of individualized medicine approaches, the continued refinement of diagnostic criteria, and the development of novel therapeutics targeting key immunological pathways [16].

EPIDEMIOLOGY AND RISK FACTORS

Incidence and Prevalence

Primary biliary cholangitis and AIH are each considered orphan diseases, with variable prevalence rates influenced by geographic, ethnic, and environmental factors. Primary biliary cholangitis is more prevalent in Northern Europe and North America, with incidence rates ranging from 0.7 to 2.7 per 100,000 person-years in these regions [17, 18]. Autoimmune hepatitis likewise exhibits a wide range of incidence rates worldwide, from 0.1 to 2 per 100,000 person-years, depending on the population studied. Notably, the overlapping PBC-AIH condition is estimated to account for 5–10% of patients with PBC, and a similar proportion of patients with AIH may show features consistent with PBC overlap [19].

Demographic Features

A pronounced female preponderance is seen in both PBC and AIH, and the same is generally true for PBC-AIH overlap. Women typically constitute 70–90% of cases, with disease onset often occurring during middle age [20, 21]. Although disease presentation in men and younger individuals is less common, an increasing number of case reports and series highlight that no age group is entirely spared [22]. The interplay between hormonal factors and autoimmunity is believed to contribute to the marked female bias observed across these conditions [23].

Genetic Susceptibility

Family studies and genome-wide association analyses have implicated certain human leukocyte antigen (HLA) haplotypes in susceptibility to both PBC and AIH [24, 25]. HLA-DRB108, HLA-DRB103, and HLA-DRB104 have each been associated with AIH in different populations, whereas HLA-DRB108 and HLA-DRB1*11 appear to be linked to PBC risk [26]. Single-nucleotide polymorphisms (SNPs) in genes regulating immune homeostasis [e.g., cytotoxic T-lymphocyte associated protein 4 (CTLA4), interleukin (IL) 2, IL-21, and tumor necrosis factor (TNF)] have also been reported to heighten susceptibility [27]. These overlapping genetic susceptibilities may partly explain why certain individuals develop a hybrid phenotype straddling cholestatic and hepatocellular autoimmune features.

Environmental Triggers

Infection with certain viral agents (e.g., Epstein-Barr virus, cytomegalovirus, and hepatitis viruses) and exposure to xenobiotics (e.g., chemicals in cosmetics or industrial products) have been proposed as plausible triggers. Molecular mimicry, epitope spreading, and bystander activation are several immunopathological mechanisms through which these environmental factors can precipitate a breakdown of self-tolerance in genetically predisposed hosts [28]. Additionally, smoking has been linked to PBC risk, whereas data on smoking and AIH are less conclusive [29]. Overall, the role of environmental triggers in overlap syndromes remains an area of considerable interest.

Role of Hormones

Beyond genetics, hormonal influence is recognized as an important aspect of autoimmune disease pathogenesis. Women have higher baseline immune reactivity due to estrogen-mediated immunostimulatory effects, contributing to a higher predisposition to diseases like PBC and AIH [30]. Although the precise mechanism through which hormones modulate overlap syndromes is not fully characterized, the substantial female predominance points to a potential influence of estrogen and other sex hormones in disease manifestation and progression [31].

PATHOPHYSIOLOGY

The immunopathogenesis of overlapping PBC-AIH lies at the intersection of cholangiocyte and hepatocyte-directed autoimmunity. Each disease has a distinct immunological signature: PBC features a T cell–driven destruction of small intrahepatic bile ducts, while AIH involves T cell–mediated periportal hepatitis directed primarily against hepatocytes [32]. In overlap syndromes, these pathogenic processes occur concurrently or evolve sequentially in the same individual [33].

Immunological and Genetic Factors

$CD4^+$ and $CD8^+$ T Cells

In PBC, autoreactive T cells, both CD4+ and CD8+, orchestrate cholangiocyte damage, particularly against the

pyruvate dehydrogenase complex E2 subunit (PDC-E2) [34]. CD8+ T cells infiltrate portal tracts and damage bile ducts through cytotoxic mechanisms [35]. Conversely, AIH is characterized by hepatocyte-directed T cells that produce interface hepatitis, with infiltration at the limiting plate. In overlap syndromes, it is plausible that some autoreactive T cells may cross-react with antigens shared by both cholangiocytes and hepatocytes, thereby amplifying inflammation in both compartments [36].

B Cells and Immunoglobulins

B cells and plasma cells are critical effectors of both humoral autoimmunity and cellular cross-talk. B cells secrete autoantibodies (e.g., AMA, ANA, SMA), which can serve as diagnostic markers and potentially contribute to tissue damage through antibody-dependent mechanisms [37]. Polytypic hypergammaglobulinemia is common in both diseases, with IgM frequently elevated in PBC and IgG in AIH. Patients with overlap often exhibit elevated levels of both immunoglobulins, underscoring the contribution of humoral immunity to their pathogenesis [38].

Cytokines and Immune Regulation

Pro-inflammatory cytokines, including IL-6, IL-1, TNF-alpha, and interferon-gamma (IFN-γ), play instrumental roles in perpetuating the inflammatory milieu [39]. Regulatory T cells (Tregs) are generally reduced or dysfunctional in autoimmune liver diseases, undermining immune tolerance [40]. Genetic polymorphisms in IL-2 and IL-21 pathways, which are integral to T cell homeostasis, have been correlated with altered disease susceptibility and phenotype in PBC and AIH, suggesting similar vulnerabilities in overlap conditions [41].

Autoantibodies in Overlap Syndrome

Autoantibodies are hallmark features of autoimmune liver disease, aiding in diagnosis and sometimes correlating with specific subtypes or prognoses.

• **Anti-mitochondrial antibody:** Nearly 90–95% of classic PBC patients test positive for AMA, with the M2 subtype (AMA-M2) most commonly associated [42].

• **Antinuclear antibody and anti-smooth muscle antibody:** ANA and SMA are frequently seen in AIH, alongside elevated IgG levels [43].

• **Additional Autoantibodies:** less commonly, anti-LKM-1 (particularly in AIH type 2) and anti-soluble liver antigen (anti-SLA) can be detected [44].

In overlapping PBC-AIH, patients often present with a mixed serological profile, such as concurrent AMA-M2 and ANA positivity. This combination, alongside elevations in both cholestatic (alkaline phosphatase) and aminotransaminases, raises the suspicion of overlap syndrome [45]. Although the exact pathological contribution of these autoantibodies remains an area of active investigation, their presence is invaluable for disease classification and monitoring [46].

CLINICAL PRESENTATION

Overlapping PBC-AIH typically merges the characteristic features of both diseases, resulting in a heterogeneous clinical picture. While some patients might present with pronounced cholestasis (pruritus, jaundice, elevated alkaline phosphatase), others may manifest a more hepatocellular pattern (fatigue, elevated transaminases, possible acute hepatitis-like episodes) [47].

Signs and Symptoms

• **Fatigue:** a common complaint in both PBC and AIH, often disproportionate to the degree of liver injury on laboratory tests [48].

• **Pruritus:** more characteristic of cholestatic disorders like PBC, though pruritus may also occur in advanced AIH or other chronic liver diseases. In overlap, pruritus can be severe and profoundly affect quality of life [49].

• **Right upper quadrant discomfort:** non-specific hepatic tenderness can occur, potentially reflecting significant hepatic inflammation or distension of the liver capsule [50].

• **Jaundice:** although typically a later feature, jaundice can appear earlier if cholestasis is pronounced, or if overlap is associated with fulminant flare-ups resembling severe AIH [51].

As cirrhosis develops, complications such as ascites, variceal bleeding, and hepatic encephalopathy may dominate the clinical scenario, underlining the importance of early detection and management [52].

LABORATORY FINDINGS AND SEROLOGY

Liver Function Tests:

• **Cholestatic pattern:** elevated alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) [52].

• **Hepatocellular pattern:** elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) [53].

• **Overlap pattern:** elevations in both cholestatic and hepatocellular enzymes [54].

• Immunoglobulin levels:

• **IgM:** characteristically elevated in PBC [55].

• **IgG:** Elevated in AIH [56].

• **Overlap:** concomitant rises in IgM and IgG [16].

• Autoantibodies:

• **AMA/AMA-M2:** diagnostic of PBC in most cases [57].

• **ANA/SMA:** associated with AIH, also found in about 30% of PBC patients but typically lower titers unless overlap is present [58].

Overlapping PBC-AIH may also feature significant fluctuations in biochemical markers over time, reflecting the dynamic interplay between cholangiopathic and hepatocellular injury [59].

DIAGNOSTIC CRITERIA AND TOOLS

Arriving at an accurate diagnosis of overlapping PBC-AIH can be challenging, given the lack of universally accepted, rigid definitions and the significant heterogeneity in clinical presentation. Nonetheless, structured criteria and multimodal evaluations—encompassing clinical, biochemical, serologic, and histologic findings - are integral to a robust diagnostic workup [60] (Fig. 1).

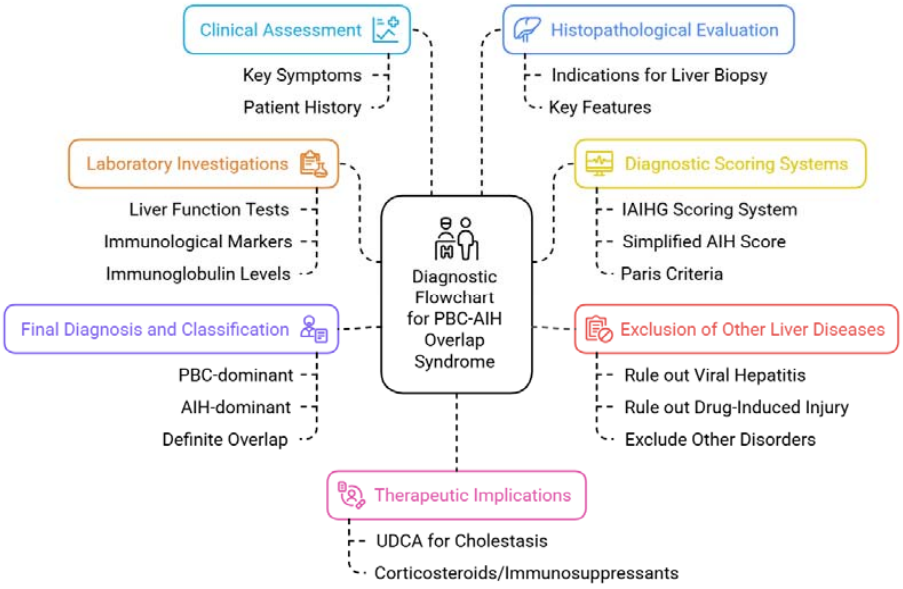

Fig. 1. Diagnostic flowchart for PBC-AIH overlap syndrome.

Histopathological Features

Liver biopsy remains the gold standard for diagnosing overlap syndromes [61-63]. Key diagnostic patterns include:

Chronic nonsuppurative destructive cholangitis (CNSDC): this hallmark of PBC involves destruction of small intrahepatic bile ducts, often with granulomatous inflammation [63].

Interface hepatitis: Characteristic of AIH, with periportal or peri-septal lymphoplasmacytic infiltrates attacking the limiting plate [61].

Coexisting lesions: In overlap syndromes, biopsy may reveal prominent interface hepatitis alongside damaged bile ducts consistent with PBC [62].

Evaluating the relative severity of bile duct damage versus interface hepatitis can guide therapeutic decisions, as patients with predominant AIH features may benefit from more aggressive immunosuppression (Fig. 2) [63].

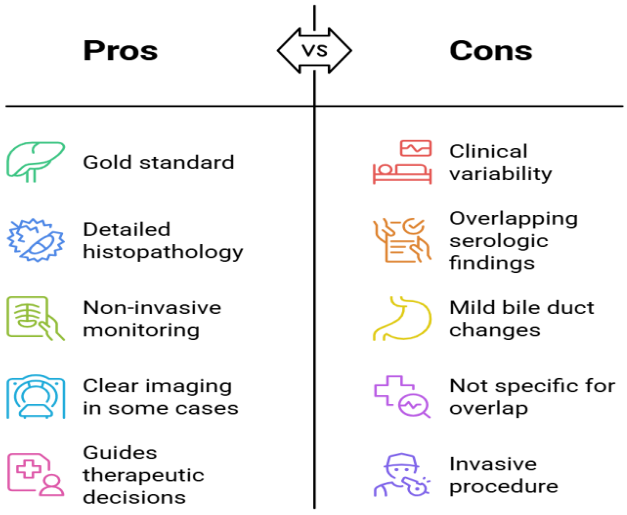

Fig. 2. Diagnosing overlapping PBC-AIH

Imaging Studies

While ultrasound is commonly used to exclude biliary obstruction, magnetic resonance cholangiopancreatography (MRCP) can sometimes delineate subtle bile duct irregularities more clearly. However, bile duct changes in PBC are often milder than in primary sclerosing cholangitis (PSC) [64]. Transient elastography (FibroScan) offers a noninvasive measure of liver stiffness, which correlates with fibrosis. Its utility lies in monitoring disease progression or response to therapy but is not specific for diagnosing overlap [65].

CURRENT CLASSIFICATION CRITERIA

International Autoimmune Hepatitis Group (IAIHG) Score

The original and revised IAIHG scoring systems incorporate autoantibody profiles, immunoglobulin levels, histology, viral serologic exclusions, and clinical features. Although developed specifically for AIH, elevated scores in a patient with PBC features may suggest significant AIH overlap [66].

Simplified AIH Score

This user-friendly iteration focuses on ANA/SMA titers, IgG levels, histology, and exclusion of viral hepatitis. It is valuable in routine practice but may not detect subtler overlaps, particularly in atypical presentations [67].

Paris Criteria

Developed specifically for PBC-AIH overlap, the Paris criteria propose that a PBC diagnosis (based on histology, AMA positivity, and elevated ALP) plus at least two of three AIH features (ALT≥5x upper limit of normal, IgG≥2x upper limit of normal, interface hepatitis on histology, or positive SMA) be present. This approach is widely accepted for classifying overlap syndromes in clinical trials and practice (Table I) [68].

Table I. Key diagnostic criteria for overlapping PBC-AIH

Criteria	Key Components	Utility
IAIHG Score	Autoantibodies, IgG levels, histology, exclusion of viral hepatitis, clinical context	Comprehensive; recognized standard for AIH; can suggest overlap when PBC features also exist
Simplified AIH Score	ANA/SMA titers, IgG level, histology, viral exclusion	More accessible for routine use; may miss partial or atypical overlaps
Paris Criteria for PBC-AIH	Established PBC + ≥2 of the following AIH indicators (high ALT, high IgG, interface hepatitis)	Specifically validated for PBC-AIH overlap; aids classification in clinical practice and trials

AIH: autoimmune hepatitis; ANA: anti-nuclear antibody; IAIHG: International Autoimmune Hepatitis Group; IgG: immunoglobulin G; PBC: primary biliary cholangitis; SMA: anti-smooth muscle antibody.

THERAPEUTIC APPROACHES

Management strategies for overlapping PBC-AIH must address both cholestatic and hepatocellular components of the disease. Optimizing therapy can be complex, as insufficient immunosuppression risks persistent inflammatory injury to hepatocytes, while neglecting cholestatic components can worsen ductopenia and fibrosis [25].

Pharmacologic Therapy

Ursodeoxycholic Acid (UDCA)

UDCA is the foundation of PBC treatment and remains a first-line agent in overlap syndromes. By replacing more toxic hydrophobic bile acids, UDCA helps mitigate cholestatic injury, stabilizes liver biochemistry, and can slow fibrosis progression. Although its role in alleviating AIH-driven inflammation is limited, UDCA is typically continued alongside immunosuppressants, as improved cholestasis can reduce pruritus and protect against ongoing biliary damage [69].

Immunosuppressive Therapy

Corticosteroids

• **Prednisone:** conventional induction therapy for AIH, often used in overlap with moderate to severe inflammatory activity (i.e., elevated transaminases, histological interface hepatitis) [12].

• **Budesonide:** an alternative corticosteroid with extensive first-pass metabolism in the liver, potentially offering fewer systemic side effects than prednisone. However, its use in patients with significant cirrhosis or portal hypertension is less favorable due to potential reduced metabolic clearance [70].

Steroid-Sparing Agents

• **Azathioprine:** Classic adjunct to maintain remission in AIH and reduce steroid dosage. In PBC-AIH overlap, azathioprine is often introduced if significant interface hepatitis persists or if steroid tapering is necessary [71].

• **Mycophenolate Mofetil (MMF):** Used in cases where azathioprine is poorly tolerated or contraindicated. Some evidence suggests improved biochemical control in refractory AIH and potential utility in overlap scenarios [72].

• **Tacrolimus and Cyclosporine:** Calcineurin inhibitors may be employed in refractory cases, although their side-effect profiles warrant caution and close monitoring.

Second-Line and Experimental Therapies

• **Obeticholic Acid (OCA):** A farnesoid X receptor agonist approved for second-line PBC therapy, especially in patients with incomplete responses or intolerance to UDCA. Its potential in overlap syndromes is under investigation, though initial data suggest some benefit for cholestatic components [73].

• **Fibrates (e.g., Bezafibrate):** may enhance the effect of UDCA and improve cholestasis in PBC. They can be considered if patients show inadequate response to UDCA, although data specifically for overlap syndromes are limited [74].

• **Biological agents (e.g., Rituximab, Anti-TNF, Anti-IL-2 Receptor):** Investigational in refractory AIH and PBC. While promising, safety and efficacy data in PBC-AIH overlap are sparse, necessitating controlled trials to clarify their role [75].

Combination Therapy and Emerging Agents

A common regimen for overlap is UDCA combined with low-to-moderate doses of corticosteroids to target both cholestasis and interface hepatitis. Azathioprine or other immunosuppressants may be added for long-term control, particularly in patients with severe inflammation, high transaminases, or inadequate response to initial therapy [76]. The emergence of new agents targeting immune checkpoints (e.g., CTLA4, PD-1/PD-L1) and specific cytokine pathways (e.g., IL-17, IL-23) hints at the future potential of more tailored immunomodulation in autoimmune liver disease. Nonetheless, the cost, safety, and real-world efficacy of these cutting-edge therapies remain under evaluation (Table II) [77].

Non-Pharmacological Management

• **Lifestyle Modifications:** Abstinence from alcohol, a balanced diet, and regular exercise can help mitigate additional liver damage and improve overall health [78].

• **Management of Pruritus:** Bile acid sequestrants (e.g., cholestyramine) often constitute first-line therapy. Other options include antihistamines, rifampin, naltrexone, and sertraline. Recently, selective ileal bile acid transporter (IBAT) inhibitors have been studied, potentially offering new avenues for refractory cases [79].

• **Nutritional Support:** Patients with advanced liver disease may be prone to malabsorption of fat-soluble vitamins, particularly in cholestatic conditions. Supplementation with vitamins A, D, E, and K may be necessary to prevent deficiency-related complications [74].

PROGNOSIS AND OUTCOME

Disease Progression and Complications

Overlapping PBC and AIH often exhibit a more severe disease trajectory, with synergy between cholestatic and

Table II. Summary of key therapeutic agents and their roles in PBC-AIH overlap

Therapeutic agent	Mechanism/Primary target	Clinical role in overlap
UDCA	Replaces toxic bile acids, reduces cholestasis	First-line for cholestatic component, combined with immunosuppression for overlap
Corticosteroids	Anti-inflammatory, broad immunosuppression	Induction therapy for moderate-severe inflammatory activity
Azathioprine	Antiproliferative, reduces lymphocyte proliferation	Steroid-sparing, long-term immunosuppression
Mycophenolate Mofetil	Inhibits inosine monophosphate dehydrogenase, reduces lymphocytes	Alternative for azathioprine intolerance or inefficacy
Obeticholic Acid	Farnesoid X receptor agonist, reduces bile acid toxicity	Second-line in PBC; emerging data in overlaps
Fibrates	Activate peroxisome proliferator-activated receptors (PPARs)	Adjunctive therapy for cholestasis in UDCA partial responders
Biologics (e.g., Rituximab)	Target B cells or cytokines	Investigational; used in refractory cases, require more evidence

UDCA: ursodeoxycholic acid. For the rest of abbreviations see Table I.

necroinflammatory damage accelerating fibrogenesis [80]. Persistent cholestasis and recurrent interface hepatitis further compromise hepatic reserve, culminating in suboptimal long-term survival if left unchecked [81]. Timely recognition, guided by histological staging and serological profiles, is crucial to prevent cirrhosis, portal hypertension, and hepatic decompensation [82]. Inadequate or delayed therapy significantly raises the risk of end-stage liver disease, necessitating liver transplantation [83]. Although combination regimens can achieve sustained remission in a subset of patients, variable responses underscore the need for vigilant monitoring and timely therapeutic adjustment [84].

Role of Follow-up and Biomarkers

Continuous evaluation through biochemical markers (e.g., ALP, IgG), imaging modalities (e.g., transient elastography), and immunological assays (e.g., autoantibody titers) is essential for guiding therapy escalation or de-escalation [85]. Novel biomarkers, including enhanced liver fibrosis (ELF) scores, microRNA signatures, and immunogenetic profiling, offer potential to stratify risk and detect subclinical disease flares [86]. Regular follow-up facilitates individualized treatment protocols, optimizing disease control and quality of life [15]. Ultimately, multidisciplinary collaboration - encompassing hepatology, pathology, and allied specialties - can enhance long-term prognosis and mitigate chronic complications [87].

SPECIAL POPULATIONS

Pediatric Overlaps

Overlapping PBC and AIH is extremely uncommon in children, as PBC itself rarely occurs in pediatric populations. Nevertheless, case reports indicate that pediatric patients can manifest characteristic cholestatic and hepatocellular lesions, reflecting an overlap phenotype. Symptoms often skew toward an acute hepatitis-like presentation, underscoring the need for early recognition and histological confirmation [88]. Therapeutic principles mirror adult protocols, with UDCA and immunosuppressive agents (e.g., corticosteroids, azathioprine) administered according to pediatric dosage guidelines [32]. Close, lifelong follow-up is critical to monitor for evolving hepatic injury, progression to advanced fibrosis, or the eventual necessity for transplantation [89]. Collaboration across pediatric hepatology, gastroenterology, and transplant services remains paramount to ensure comprehensive care and optimize outcomes in this unique patient population [78].

Pregnancy Considerations

Autoimmune liver diseases can profoundly shape pregnancy outcomes, and conversely, gestational immunological changes may worsen or ameliorate disease activity [90]. In overlapping PBC-AIH, some women experience exacerbated cholestasis or postpartum flares, necessitating vigilant biochemical monitoring throughout pregnancy and after delivery [91]. Ursodeoxycholic acid remains key for controlling pruritus and cholestasis, while prednisone, typically used for acute flares, is generally considered safe with cautious monitoring. Azathioprine may be continued under careful risk-benefit evaluation [92, 93]. Ultimately, coordinated management by hepatologists and obstetricians ensures prompt detection of flares, safeguarding maternal-fetal well-being.

CONCLUSIONS

Overlapping PBC and AIH is a complex autoimmune disorder that simultaneously involves cholestatic and hepatocellular damage, resulting in an accelerated disease course if unrecognized. The Paris criteria and the IAIHG scoring systems, complemented by histopathological analysis, remain pivotal in distinguishing PBC-AIH from the classic forms of each disease. Therapeutic strategies typically combine UDCA to mitigate cholestasis with immunosuppressants to control interface hepatitis, thus addressing the dual pathological processes. Ongoing assessment of clinical status and biochemical markers, including immunoglobulins and autoantibodies, informs therapy adjustments and helps prevent progressive fibrosis or cirrhosis. A multidisciplinary approach - incorporating hepatology, pathology, and other subspecialties - ensures comprehensive patient management,

timely identification of disease flares, and better long-term outcomes. Such targeted intervention strategies optimize care and enhance quality of life by attenuating the risk of advanced liver disease. Vigilance and optimized therapeutic regimens are essential to maintain disease control.

Conflicts of interest: None to declare.

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