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# Primary Biliary Cholangitis (PBC): Prognosis and Treatment Procedures

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**Abstract**

Primary biliary cholangitis (PBC) is a chronic non-supportive destructive intrahepatic autoimmune cholangitis liver disease. The proper reason of development of this disease is unknown. However, in most cases it develops when an individual's immune system attacks and destroys the small and medium-sized bile ducts inside the liver. The PBC causes liver inflammation, fibrosis, portal hypertension, progressive cirrhosis, and liver failure over time if the disease is left untreated. Usually, it affects women between the ages of 40 and 60, but it has been diagnosed outside of this age range, as well as in men with a male-to-female ratio of 1:10. The increased incidence of the disease is visible in the developed countries; however, the prevalence of it in developing countries is increasing presumably due to the growth in recognition and knowledge of the disease. Although most patients are asymptomatic at first presentation, typical patients show symptoms of fatigue, itching, and jaundice. There is no cure for PBC, but treatment can help slow the progression of disease and associated symptoms. Ursodeoxycholic acid (UDCA) and obeticholic acid (OCA) are currently the only recommended therapies of it and a patient survives as long as age- and sex-matched healthy subjects. The ultimate goal of treatment of PBC is improvement of health-related quality of life for all patients with a proper care of related symptoms, such as fatigue and itching. In this study an attempt has been taken to discuss the prognosis and treatment procedures of the disease PBC for the welfare of the patients.

**Keywords:** primary biliary cholangitis, AMA, ursodeoxycholic acid, obeticholic acid

## 1. Introduction

The liver is an essential organ in the human body that performs up to 500 different vital functions in combination with other organs and systems, such as supporting digestion, immunity, proteins synthesis, amino acid metabolism, blood coagulation, detoxification, vitamin storage, etc. (Hettiaratchi, 2022). A healthy liver is necessary for survival. The liver produces bile, a yellow-green fluid that is stored in the gall bladder and added to the digestive tract via bile ducts (Mohajan, 2025b). The liver helps to break down food and converts into nutrients and energy, store carbohydrates and maintaining a good balance of glucose levels in the blood, makes new proteins, such as clotting factors and immune factors that support muscle and immune system,

metabolizes drugs, and stores nutrients and energy (Kalra et al., 2022). It metabolizes xenobiotic and endogenous hormones, and waste products; and produces bile to aid digestion and as route of excretion of liver waste. It also removes waste products which the kidneys cannot remove, such as fats, cholesterol, toxins, and medications (Ebrahimkhani et al., 2014). The retained substances are harmful to the liver and worsen the inflammation which leads to further damage. This can over time result in scarring of the liver. When there is a lot of scarring in the liver this is called cirrhosis (Chiang, 2014).

Primary biliary cholangitis (PBC) is a rare chronic cholestatic liver disease belonging to cholangiopathies that affects the expectation of life of a patient. It is characterized by the damage and loss of the epithelial lining of small and medium-sized intrahepatic bile ducts, leading to ductopenia and cholestasis (Reshetnyak et al., 2025). When the bile ducts are damaged, bile and other substances cannot be eliminated and accumulate in the liver. It is a non-supportive and destructive cholangitis that attacks the adjacent hepatic parenchyma, and without treatment it gradually advances to fibrosis and cirrhosis, and sometimes requires liver transplantation over a period of 10 to 20 years. There is no cure of this disease, but treatment can help slow the progression of disease and alleviate symptoms. Over time, it leads scarring, and in the terminal stage liver cirrhosis and liver failure develops (Boonstra et al., 2012). It is a relatively rare disease, affecting up to one in 3,000-4,000 people, and much more common in women, with a sex ratio of 10:1 female to male. Usually, children are virtually never diagnosed with this disease (Carbone et al., 2013). The increased incidence of the disease is visible in the developed countries, such as in the United Kingdom, the USA, Japan, and Australia, and least common in black Africans (Prince & James, 2003).

The exact cause of PBC is unknown. Most research suggests that the reason of development of this disease is the presence of anti-mitochondrial antibodies (AMAs) (Xiang et al., 2017). Common symptoms of this disease are fatigue, itching, and in more advanced stage jaundice. Ursodeoxycholic acid (UDCA) and obeticholic acid (OCA) are currently the only recommended therapies of the treatment of PBC. Patients with a good response to UDCA survive as long as age- and sex-matched healthy subjects (Al-Harthy & Kumagi, 2012).

## 2. Literature Review

A literature review is a careful survey and critical summary of previously published researches on a particular subject area within a certain time period that combines both summary and synthesis (Cooper, 1998). The main focus of an academic research paper is to develop a new argument, which contains a literature review as one of its parts. The literature review summarizes and synthesizes the arguments and ideas of others without adding new contributions (Shields & Rangarjan, 2013). It provides the researchers and the audiences with general information of an existing knowledge of a particular topic. A good literature review has a proper research question, a proper theoretical framework, and a chosen research methodology (George et al., 2023).

Vasiliy Ivanovich Reshetnyak and his coauthors have presented the historical aspects of PBC along with the evolution of its nomenclature. They have shown the importance of the development and the evolution of clinical, laboratory, and instrumental methods for the discovery and elucidation of the pathophysiological mechanisms of this disease (Reshetnyak et al., 2025). Cynthia Levy and her coworkers have observed that people living with PBC are frequently symptomatic; experiencing a quality-of-life burden dominated by fatigue, itchy, abdominal pain, and sicca complex. They have explained that first-line therapy is a non-specific anti-cholestatic agent, ursodeoxycholic acid; obeticholic acid is a semisynthetic farnesoid X receptor agonist adds choleretic, anti-fibrotic, and anti-inflammatory activity; and proliferator activated receptor (PPAR) is a pathway agonist, which are taken to care all patients with PBC (Levy et al., 2023). Hirsh D. Trivedi and his coauthors have noticed that pruritus affects 60-70% of individuals with PBC that leads to sleep disturbances, fatigue, depression, and suicidal ideation. They have outlined the emerging treatment modalities for patients with PBC who have pruritus (Trivedi et al., 2017). Annarosa Floreani and Sara De Martin have offered an overview on the experimental pharmacological strategies currently exploited for PSC treatment. Currently, there is no effective treatment which can delay its progression or ameliorate the transplant-free survival. They have realized that novel pharmacological agents emerged through the modulation of bile composition, immunomodulation, targeting the gut

microbiome, and targeting fibrosis (Floreani & De Martin, 2021).

Atsushi Tanaka and his coworkers have stressed on the improvement of health-related quality of life with better recognition and care of subjective symptoms, such as pruritus and fatigue, and is also an important treatment goal for PBC patients (Tanaka et al., 2018). Frederik Nevens and his coworkers have shown that the discovery of nuclear receptors and transporters, such as second-line therapies have contributed to the development of new drugs for the treatment of cholestatic liver diseases (Nevens et al., 2023). Maria Guarino has shown that PBC is a chronic autoimmune disease resulting in the destruction of the small bile ducts in the liver. The PBC is a condition with a heterogeneous and poorly characterized phenotype for which limited therapeutic options are currently available (Guarino, 2018). Elias Kouroumalis and George Notas have examined various epidemiological and geoepidemiological data as well as the complex pathogenetic aspects of PBC, focusing on recent in vivo and in vitro studies with clinical characteristics of this disease (Kouroumalis & Notas, 2015).

**3. Research Methodology of the Study**

Research is a careful and organized study of a subject to find new facts, test ideas, and solve problems to build true knowledge. It is a creative and systematic work undertaken to increase the stock of knowledge (Cohen & Arieli, 2011). It is an art of scientific investigation to generate new knowledge through a systematic and orderly collection, organization, and analysis of information with an ultimate goal of making the research useful in decision-making (Kabir, 2016). A good research is systematic, logical, empirical, and replicable. It can be classified as basic, applied, and evaluative. On the basis of method, it can be classified as historical, descriptive, correlational, ex-post facto, and experimental (Creswell, 2014). A methodology is the overarching strategy, framework, and theoretical analysis that guides how a project, study, and research goal is carried out. Traditionally it can be divided into quantitative and qualitative methodologies (Herrman, 2009). The quantitative character is of the natural science that uses precise numerical measurements, and qualitative is of more characteristic of the social sciences that aims more at an in-depth understanding of the meaning of the studied phenomena and less at universal and predictive laws (Berg, 2009). Therefore, a research methodology is a structured and scientific approach used to collect, analyze, and interpret quantitative or qualitative data to answer research questions or test hypotheses (Silverman, 2011).

A researcher faces numerous problems during data collection, statistical designs, and finally to prepare a seminal research work (Mohajan, 2020). In this study secondary data are used to develop this article. We have prepared this paper by consulting the books, journals, handbooks, theses of famous authors; and by taking the help from the internet, websites, etc. (Mohajan, 2018a). The reliability and validity are essential issues in any research. In this article we have tried our best to maintain the reliability and validity throughout of the research work (Mohajan, 2017). We have organized the paper systematically as: liver and its functions are discussed in briefly; historical background, causes, symptom, diagnose, and treatment of PBC are included for the benefit of the patients. Finally, we have stressed on the proper diet and nutrition management for the welfare of the PBC patients (Mohajan, 2018b).

**4. Objective of the Study**

The PBC is a chronic progressive cholestatic granulomatous and destructive inflammatory lesion of small intralobular and septal bile duct, which is ten times more common in women than men. It is a rare autoimmune cholestatic liver disease, and high titer anti-mitochondrial (AMA) and nuclear dots antinuclear (ANA) autoantibodies are related to this disease (Carey et al., 2015). It is more common in people who have a parent or sibling, particularly an identical twin with the disease. It is heterogeneous in its pre-sensation, symptomatology, disease progression and response to therapy. Without effective treatment, the disease progression frequently leads to liver failure and death (Guarino, 2018). The environmental factors, such as exposure to toxic chemicals, smoking, and infections may trigger or worsen the disease (Smyk et al., 2011). The Sjögren's syndrome, keratoconjunctivitis sicca, Hashimoto's thyroiditis, rheumatoid arthritis, and scleroderma are seen among some PBC patients that are related to genetics (Carey et al., 2015).

Many PBC patients are asymptomatic and their condition is discovered through general screening blood tests for unrelated problems. However, usual clinical presentations are pruritus and fatigue with significant elevations of

alkaline phosphatase (ALP) and gama glutamyl transferase (GGT) (Walker et al., 1965). Other symptoms of this disease are weight loss, xanthelasma, ascites, hepatosplenomegaly, jaundice, and signs of hepatic encephalopathy, and sometimes steatorrhea and osteoporosis may occur with bone pain or pathologic fractures (Kaplan & Gershwin, 2005). Main objective of this article is to discuss the basic concepts of PBC and an overview of the current treatment options and future opportunities for patients with PBC to improve the quality of life for patients with this disease. Other minor objectives of the study are as follows:

1) to highlight on liver and its functions, and historical background of PBC,
2) to focus on causes, symptoms, and diagnosis of PBC, and
3) to show the treatment and nutrition of PBC.

**5. Liver and Its Functions**

Liver is a wedge shaped dark pinkish-brown largest internal organ, and in an average adult human weighs 1.5-2.0 kg (Mohajan, 2025b). It is divided into right and left lobes; the right lobe being larger than the left. It is situated in the right upper quadrant of the abdomen and extents across the midline to the left upper quadrant (Juza & Pauli, 2014). It is considered as the site of the soul, and the central place of all forms of mental and emotional activity. It is the powerhouse of the body for metabolism and a center for numerous physiological processes (Mohajan, 2025a).

Liver plays an important role in metabolism through the preservation and regulation of the levels of lipid and glucose in the body as well as energy metabolism. It performs a wide range of vital functions, such as blood detoxification and purification; synthesis of plasma proteins; production of bile; the metabolism of carbohydrates, fats and proteins, etc. (Sumadewi, 2023). It can regenerate most of its own cells when they become damaged. However, if injury to the liver is too severe or long lasting and scar tissues are created, and the scarring of the liver may lead to cirrhosis. At the end-stage of liver disease, the liver can no longer perform important functions (Kouroumalis & Notas, 2015).

The functions of liver in brief are metabolism of carbohydrates, proteins and fat; storage of glycogen, vitamins (e.g., A, D, E, K), minerals (e.g., iron and copper); detoxification of drugs and toxins; excretion of bile and urea; reservoir of blood (Ozougwu, 2014); filtration of bacteria, degradation of endotoxins and lactate metabolism; immunological functions with synthesis of immunoglobulins and phagocytic action by Kupffer cells; and haemopoeisis in the foetus (Katawala, 2024). The liver plays an active role during digestion through the production of bile that is a mixture of water, bile salts, drugs and hormones, cholesterol, bilirubin, fats, and fluids. Bile helps the body to absorb fats, cholesterol, and fat-soluble vitamins (Alamri, 2018). The bile ducts carry bile from the liver to the gallbladder and stored there, and then transfer the bile to duodenum and use in digestion of foods (Puestow, 1931). The bile carries cholesterol, toxins, and waste products to the intestines to remove them. When bile ducts are damaged, bile and toxic wastes are built up in the liver and damage liver tissue (Chiang, 2014).

**6. Historical Background**

In 1761, Italian anatomist Giovanni Battista Morgagni (1682-1771) first observed abnormal human liver but could not provide proper reason of this abnormality. In 1851, two English physicians Thomas Addison (1795-1860) and William Withey Gull (1816-1890) drew attention to some unusual, rare skin lesions and introduced the term "Vitiligoidea" to describe them (Reuben, 2003). They have first described a clinical picture of progressive jaundice in the absence of mechanical obstruction of the large bile ducts, basis on a case report of a 42-year-old female who developed jaundice and xanthoma. It was the first published report of a patient with obstructive jaundice without evidence of large bile duct abnormalities (Addison & Gull, 1851). In 1892, French hepatologist Victor Charles Hanot (1844-1896) discussed the signs of chronic liver disease and cirrhosis, including hepatomegaly with chronic jaundice (Hanot, 1892).

In 1949, in a landmark paper of US pathologist H. E. MacMahon and US physician S. J. Thannhauser proposed the term "xanthomatous biliary cirrhosis" for the disease PBC (MacMahon & Thannhauser, 1949). Later in 1950, American physician Edward Henry Ahrens (1915-2000) and his coauthors have reported on a group of older women with progressive jaundice, pruritus, and hepatosplenomegaly; and have coined the term "primary biliary cirrhosis", which was more readily accepted by clinicians (Walker et al.,

1965).

The basic histological description as chronic intrahepatic non-supportive destructive cholangitis was reported by Emanuel Rubin and his coauthors in 1965 (Rubin et al., 1965). A major turning point occurred in 1965 when English physician J. G. Walker and his colleagues revolutionized the diagnosis and discovery of Antimitochondrial Antibodies (AMAs) in the blood of patients with the PBC (Walker et al., 1965). They have found this blood marker among more than 90% of patients, and have revealed that it is an autoimmune condition in which the body's immune system mistakenly attacks its own bile ducts that has dawn of a new era in PBC research world. Since then, the understanding of PBC has changed entirely (Tanaka et al., 2018). As the term "cirrhosis" has the stigmata for alcohol abuse, international experts in the field of hepatology the disease is renamed "primary biliary cholangitis" retaining the abbreviation PBC in 2014, where cholangitis means inflammation of the bile ducts. It reflects the natural progression of the disease and describes the condition more accurately than the former term (Beuers et al., 2015).

Ursodeoxycholic acid (UDCA) is a naturally occurring bile acid used to dissolve cholesterol gallstones and treats chronic liver diseases. For centuries, traditional Chinese doctors have used it to treat hepatobiliary disease collecting from adult bears (Lazaridis et al., 2001). In the 20$^{th}$ century, Swedish biochemist Olof Hammarsten (1841-1932) isolated a new bile acid from a polar bear and named it "ursocholeinsäure". In 1927, Japanese researcher Masato Shoda first describes the chemical form of it and named it ursodeoxycholic acid (Poupon et al., 1987). The UDCA works by reducing the amount of cholesterol absorbed by the body and secreted into the bile, allowing gallstones to gradually dissolve and protecting liver cells from toxic bile acids (Makino & Tanaka, 1998).

**7. Causes of PBC**

The exact pathogenesis of PBC is unknown to the researchers and physicians. Most research suggests that the reason of development of this disease is a combination of multiple genetic factors, epigenetic factors, and superimposed environmental triggers. Smoking, urinary tract infections, nail polish, and hair dyes are significantly associated with increased risk of PBC (Hirschfield & Gershwin, 2013). Among most of the patients, PBC is developed due to the presence of anti-mitochondrial antibodies (AMAs) that target mitochondrial enzymes 2-oxo acid dehydrogenase complexes (2-OADCs) (Xiang et al., 2017). The presence of AMAs is a clinical hall mark and important diagnostic feature of PBC that is found in about 95% of patients. Non-specific antinuclear antibodies (ANAs), such as proteins in the forms anti-Sp100 and anti-gp210 are found in at least 30% of PBC sera, and can be used as markers of PBC when AMAs are absent (Guarino, 2018). There is no evidence that PBC is inherited from mother to child and it is not caused by alcohol consumption, and genetic factors can increase a person's risk (French et al., 2022).

**8. Symptoms of PBC**

Symptoms of PBC vary from person to person with mild to severe. Many people with PBC can be symptom-free for years. Chronic worsening fatigue is usually the first and commonest presentation of PBC (Swain & Jones, 2019). Classic symptoms of it are fatigue and pruritus. Common symptoms of PBC are depression, hypothyroidism, cognitive decline, anaemia, sleep disturbance, obesity, social and emotional dysfunction, hyperlipidemia, metabolic bone disease, vitamin deficiencies, and medication side-effects (Mohajan & Mohajan, 2023a,b,c). Some other symptoms of this disease are dry skin and dry eyes, itching, abdominal discomfort and pain, joints ach, unexplained weight loss, indigestion, nausea, poor appetite, bloated abdomen due to fluid buildup, abdominal pain, swollen feet, sicca complex, osteoporosis, xanthelasma, skin hyper pigmentation, and jaundice; and also vaginal dryness is noticed among women with PBC (Selmi, et al., 2011). Some patients show abnormal bleeding with pale stool and dark urine, and elevated prothrombin time. The PBC impairs bone density and the risk of fracture increases. The itching is typically mild-to-moderate in intensity and bile acids are thought to play a prominent role in mediating itching. Abnormalities in liver enzyme tests are usually present and elevated gamma-glutamyl transferase (GGT) and alkaline phosphatase (ALP) are found in early stage (Lindor et al., 2009). Elevated levels of immunoglobulin and of cholesterol are common in PBC; and change in albumin is observed with disease progression. In advanced stage, the PBC may lead to a number of complications, such as fluid retention in the abdomen, enlarged spleen, oesophageal varices,

hepatic encephalopathy, etc. Among some patients the extrahepatic autoimmune disorder, such as thyroid disease, rheumatoid arthritis, or Sjögren's syndrome can be developed (Floreani et al., 2014). Among some PBC patients, portal hypertension and esophageal varices may develop before cirrhosis. When thrombocytopenia is seen that is usually a manifestation of portal hypertension (Lindor et al., 2022).

**9. Diagnosis of PBC**

At present most of the PBC patients are diagnosed asymptomatically, when the hepatologists find abnormal liver function tests (LFTs), usually elevated gamma-glutamyl transferase (GGT), aspartate aminotransferaseto (AST), alanine aminotransferase (ALT), serum cholestatic enzymes, and alkaline phosphatase (ALP) in early stage, and elevations in bilirubin occur in advanced disease (Montano-Loza & Corpechot, 2021). The diagnostic process of PBC should be a step-by-step approach, beginning with the anamnesis and physical examination, followed by laboratory tests and non-invasive assessment, and finishing with liver biopsy if necessary (Guarino, 2018). The differential diagnoses of the PBC are cholestatic drug reaction, biliary obstruction, sarcoidosis, autoimmune hepatitis, and primary sclerosing cholangitis (Al-Harthy & Kumagi, 2012). A thorough history and physical examination, serological test, abdominal ultrasound, x-rays, magnetic resonance imaging (MRI), and a computed tomography (CT) scan are usually performed to rule out blockage to the bile ducts. A liver biopsy is needed if uncertainty of the disease remains among some patients when PBC-specific antibodies are absent (Reshetnyak et al., 2025). It is also useful to stage the disease for fibrosis and ductopenia through the liver stiffness measurement (LSM). Sometimes an endoscopic retrograde cholangiopancreatography of the bile duct may be performed (Nakamura et al., 2007). A liver biopsy can confirm the diagnosis of PBC if the AMA blood test is negative and the person shows other signs of PBC. A Fibroscan test is done to get information as to how stiff the liver is after scarring due to PBC. Indeed, if the diagnosis is uncertain, magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde cholangiopancreatography (ERCP) may be necessary (John et al., 2022).

**10. Treatment of PBC**

The real cause of chronic and slowly progressive cholestatic liver disease PBC has not been identified and the treatment of it remains challenging (Reuben, 2003). There is no cure for PBC, but treatment can help to slow down the progression of disease and associated symptoms. Before the 1990s, the PBC was universally fatal, with a median survival of just 6 to 10 years from the time of diagnosis without therapy. Initial treatment of it was vitamin therapy, calcium supplements, bile thinners and anti-inflammatory medications, and drugs to treat itching (Carbone et al., 2013). Some factors are used for the treatment of PBC are response to treatment, demographic factors, cholestasis symptoms, serum liver tests, autoantibodies, serum markers of fibrosis, liver stiffness measurement (LSM), measurement of the hepatic venous pressure gradient (HVPG), and histologic features (Lindor et al., 2019).

*10.1 First-Line Therapy*

Before use of ursodeoxycholic acid (UDCA), an increasing serum bilirubin after a relatively stable phase was an ominous sign and death was the final event after a few months. In 1987, the German hepatologists Ulrich Leuschner and Winfried Kurtz reported a positive effect of UDCA in patients with PBC (Leuschner & Kurtz, 1987). The introduction of the UDCA in the treatment of PBC has altered the natural course of the disease and it affects positively overall and ensures liver transplant–free survival rates. The clinical trials with a naturally occurring UDCA provided the first effective treatment that improves biochemical evidence of cholestasis to slow disease progression and increase survival rates (Trivella et al., 2023). In 1927, Japanese researcher Masato Shoda became the first person to describe the chemical form of UDCA that he similarly identified in the bile of a Chinese black bear. He called this bile ursodeoxycholic acid (UDCA) because he discovered that it was a chemical isomer of deoxycholic acid (Mells et al., 2013). The UDCA has several potential mechanisms of action, such as the stimulation of biliary secretion of hydrophobic bile acids and bicarbonates, the latter serving as a shield for cholangiocytes and periportal hepatocytes from the toxic effects of endogenous bile acids, and both actions contributing to protect liver cells against bile acid induced apoptosis (Poupon, 2012).

The UDCA is a bile acid that is a metabolic derivative of the gut bacteria, which stimulates post-transcriptional signaling and insertion of transport proteins, and channels into their target membranes. It is quickly established as the first-line therapy, because it works by improving bile flow and reducing toxicity, significantly slowing disease progression, and extending the lifespan of patients to near-normal levels (Harms et al., 2018). It has three mechanisms of actions: i) protection of cholangiocytes from cytotoxicity of hydrophobic bile acids by modulating the composition of mixed phospholipidrich micelles through the reduction of bile acid cytotoxicity and concentration of hydrophobic bile acids in cholangiocytes; ii) stimulation of biliary secretion of bile acids; and iii) protection of hepatocytes against bile acid-induced apoptosis by inhibiting mitochondrial membrane permeability transition (Purohit & Cappell, 2015).

It is safe, free of substantial adverse effects, affordable for lifelong use, and is associated with an excellent tolerability profile. It can delay or eliminate the potential for PBC to progress towards liver failure and/or liver transplantation. The optimum dose of it is 13-15 mg/kg per day. Sometimes fibrate therapy is needed to improve biochemical parameters, such as alkaline phosphatase in those who are unresponsive to UDCA therapy (Reig et al. 2015). It seems to be safe during pregnancy and breast-feeding. Some patients cannot tolerate it due to side-effects, such as weight gain, diarrhea, thinning of the hair, flatulence, nausea, and vomiting (Siegel et al., 2003). Although UDCA is clearly a beneficial treatment, 30 to 40% of patients have an inadequate biochemical response to therapy, and can undergo disease progression and remains at risk of liver-related complications (Montano-Loza & Corpechot, 2021).

*10.2 Second-Line Therapy*

A second-line medications, such as obeticholic acid (OCA), an agonist of the intranuclear bile acid farnesoid X receptor (FXR), is also included in May 2016 for those who do not respond fully to UDCA that improves biochemical parameters of patients. Its administration is recommended at a dose of 5 mg with adjustment to 10 mg if applicable that can be used as a single oral daily dose or divided doses according to tolerability (Kowdley et al., 2018). The OCA is associated with a significant reduction in serum levels of ALP (about 35%) and total bilirubin (about 8%) within a year. It improves hepatic bile acid excretion and reduces exposure of hepatocytes to cytotoxic bile acids in humans (Corpechot et al., 2019). It reduces inflammation in the liver and has antifibrotic effects through inhibition of fibrosis progression, promotion of fibrosis resolution, and inhibition of hepatic stellate cell activity. In addition, it acts as a local nitric oxide donor in the liver (Goel & Kim, 2018). OCA-treated patients may exhibit alterations in serum lipid levels, such as a decrease in high-density lipoprotein (HDL) coupled with an increase in total and low-density lipoprotein (LDL) cholesterol (Dyson et al., 2015).

*10.3 Third-Line Therapy*

Peroxisome proliferator-activated receptor (PPAR) agonists signal via specific intranuclear receptors ($\alpha$, $\beta$, $\gamma$, and $\delta$ isoforms) to control diverse metabolic processes, such as lipid and bile acid metabolism that are belong to the same nuclear receptor family as FXR (Colapietro et al., 2023). It is the third treatment, after UDCA and OCA have shown clear beneficial effects in a large and well-powered, and is associated mechanistically with regulation of bile acid synthesis, metabolism, and transport. At present five PPAR agonists bezafibrate (PPAR-$\alpha$, $\beta$, $\delta$), saroglitazar (PPAR-$\alpha$, $\gamma$), Elafibranor (PPAR-$\alpha$, $\delta$), fenofibrate (PPAR-$\alpha$), and pemafibrate (PPAR-$\alpha$) are used for PBC treatment. These agonists modify bile formation and regulate inflammation and fibrosis (Mohajan & Mohajan, 2024).

*10.4 Treatment of Extrahepatic Complications*

Pruritus remains an agonizing and sometimes difficult to treat PBC patients, and chronically itchy skin is a maddening symptom. It is associated with sleep deprivation, depression, social isolation, and worse fatigue (Levy et al., 2023). Bile acid binding resin, such as cholestyramine, antihistamines, naloxone, naltrexone, gabapentin, and rifampicin are recommended as first-line therapy for reducing pruritus in PBC (Oster et al., 1965). Cholestyraminea is the bile acid sequestrant and non-absorbable anion exchange resin that represents the only approved and therefore guideline-recommended first-line treatment option for pruritus in the PBC, which is given 4–16 g/day (Lindor et al., 2019). Rifampicin is an efficient second-line agent that is an agonist of the PXR as well as able to induce important liver enzymes and transporters that holds the potential to change the hepatic metabolism and

elimination of possible pruritogens and can be used with a dose of 150–300 mg twice daily (Khurana & Singh, 2006). Hot baths and hot showers can be avoided, and also skin moisturizer medications can be used to reduce pruritus. Dry eyes and dry mouth may be relieved by artificial tears and saliva, and lubricating gels and creams (Barton-Burke et al., 2017).

*10.5 Liver Transplantation (LT)*

If all therapies have failed in patients of PBC and the liver becomes severely damaged, a liver transplantation (LT) may be necessary, and it is the only effective treatment for those with life-threatening end-stage liver disease (Khungar & Goldberg, 2016). In the 1980s and before, LT was the only therapeutic resource for patients with PBC. Fortunately, at present most people with PBC do not ever experience cirrhosis and liver failure, and do not require a LT. Up to 10% of the PBC patients need LT and the outcome after LT is generally good and improve long-term survival in PBC patients. But the rates of LT are falling due to earlier and more prompt diagnosis as well as increased use of medicines, such as UDCA, OCA and other medications (Neuberger & Jones, 2001).

**11. Diet and Nutrition of PBC**

Malnutrition is often observed in PBC patients due to malabsorption caused by lack of sufficient bile acids in the intestinal lumen, and is characterized by loss of muscle mass, fatigue, metabolic bone disease, deficiency of fat-soluble vitamins, etc. (Hammad et al., 2017). At present there is no standard PBC diet, and diet list is changed according to the disease progresses. A healthcare provider and a registered dietitian can provide an eating plan to a PBC patient. The Mediterranean diet is often considered the gold standard and typically works well for most people with PBC. But adjusting the daily diet a patient can manage PBC and keeps his/her liver healthier (Cleveland Clinic, 2026).

A healthy and well-balanced diet is important for a PBC patient for healthy liver. A PBC patient must eat from all food groups, such as plenty of fruits and vegetables which are anti-inflammatory, high in fiber, and full of important nutrients; lean protein, such as chicken, fish, beans, and lentils; healthy fats, such as nuts, seeds, olives, avocado, and oily fish; and slow-release carbohydrate foods, such as whole-meal bread, rice, pasta, and cereals (Lindor et al., 2019). The sea fishes, such as Salmon, Herring, Bluefin tuna, Halibut, Mackerel, and Anchovies that are rich in omega-3 fatty acids can help to combat inflammation and a PBC patient can eat them (Reshetnyak & Maev, 2022). Fat-soluble vitamin supplements, such as vitamins A, D, E, and K, and calcium can be prescribed; since absorption of these vitamins from food is reduced (Sokol, 1994). Low-salt nutritious diet and regular weight bearing exercise can be taken properly. Alcohol can lead to a buildup of toxins and fats in the liver, and can damage the liver; a PBC patient should avoid it (Alnounou & Munoz, 2006).

Saturated fats put extra pressure on the liver to produce bile and can also worsen inflammation that can escalate PBC and further restrict bile flow. Cut down on sugary drinks; processed foods, such as cakes, biscuits, and crisps; fatty foods, such as red meat and fast foods; and high calorie foods, such as chocolate, ice cream, soda, baked foods, and candy (Zhang et al., 2024). These foods are caused of weight gain, obesity, and diabetes; and put stress on liver (Mohajan & Mohajan, 2023a,b,c).

**12. Conclusions**

The PBC is an archetypal progressive autoimmune chronic lymphocytic cholangitis that is associated with interface hepatitis, ductopenia, cholestasis, and progressive biliary fibrosis. Although most patients are diagnosed in an advanced stage with classical signs and symptoms, such as pruritus, jaundice, and xanthomatosis; at present earlier investigations of PBC are done frequently. The introduction of UDCA, OCA, fibrates, and PPAR agonists, improvement of testing AMA profiles and increased knowledge of the disease with regular health checkup has improved the scenery of PBC, and shows hope of long-term survival. If untreated, PBC slowly progresses toward cirrhosis with all the complications, including liver transplantation and death. The future of therapy for PBC is as bright and dynamic as it ever has been and improves patient quality as well as quantity of life. We hope that the use of multiple combination therapies will significantly improve the treatment of PBC in the coming years.

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