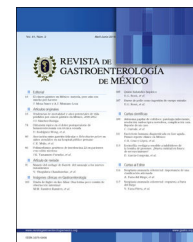




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EDITORIAL

Primary biliary cholangitis and its association with other autoimmune diseases in a Mexican cohort[☆]



Colangitis biliar primaria y su asociación con otras enfermedades autoinmunes en una cohorte mexicana

Primary biliary cholangitis (PBC), previously known as primary biliary cirrhosis, is a chronic cholestatic autoimmune disease, secondary to biliary epithelial cell damage that causes destruction of the small and medium-caliber interlobular and septal bile ducts.¹

The natural history of PBC is characterized by different phases. The first is the preclinical phase, in which there is only evidence of antimitochondrial antibodies (AMAs). The asymptomatic phase follows, with an elevated alkaline phosphatase level, which can then progress to a symptomatic phase, predominantly characterized by fatigue and pruritus. The last phase is the terminal phase, in which complications associated with the development of cirrhosis of the liver are present.²

The pathogenesis of PBC is not fully understood, but it is thought to be multifactorial. The participation of genetic, epigenetic, environmental, and even infectious factors appears to be necessary for its development. Therefore, the study of risk factors, as well as the association with other nonhepatic autoimmune diseases in different geographic areas, is most relevant.

In the present study conducted by González-Huezo et al.,³ 78 patients diagnosed with PBC at a tertiary care hospital in central Mexico were retrospectively evaluated. The authors previously excluded 36 patients due to incomplete clinical data or diagnosis of PBC-autoimmune hepatitis overlap syndrome.

Similar to that reported in other case series, the prevalence of AMAs, antinuclear antibodies (ANAs), and anti-smooth muscle antibodies (ASMA) was 95, 71, and

8%, respectively.⁴ The frequency of at least one autoimmune disease associated with PBC in that cohort was 63%, which was slightly higher than the frequency reported in other studies.^{5–9} Sjögren's syndrome was the most commonly associated autoimmune disease (30%), most likely due to the presence of chronic autoimmune epithelitis in both pathologies.¹⁰ Upon comparing the reported results with the prevalence of different extrahepatic autoimmune diseases, diverse similarities and differences were observed between the Mexican population and those of other published case series (Table 1).

The study by González-Huezo et al.³ is important because it is the largest cohort of patients with PBC in Mexico in which the association with other autoimmune diseases has been studied. However, its limitations were the fact that it was a retrospective analysis and that the patients came from a tertiary care hospital center with a high referral rate of rheumatologic diseases.

The predominance of PBC and other autoimmune diseases in female patients in the present study, as well as in other case series, appears to be associated with the increase in sex chromosome alterations, including epigenetic mutations and alterations in the X chromosome.¹¹ Even though the presence of an uncontrolled autoimmune disease confers a worse prognosis on patients with PBC, the coexistence of PBC with other autoimmune diseases is not generally associated with a greater risk for progression to cirrhosis of the liver or a lower survival rate.⁵ In fact, some studies have reported less severity in both diseases when they present together.

Prognosis for patients with PBC is varied, resulting in the development of different scales for predicting survival in patients with PBC, whether untreated (Mayo score) or after beginning treatment with ursodeoxycholic acid (UDCA), or whether in early stages (I and II) (Paris II) or advanced stages (III and IV) (Paris I). Other scales were recently developed

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Table 1 The main studies evaluating the presence of extrahepatic autoimmune diseases in patients with primary biliary cholangitis.

Author/year/country	Number of patients	Extrahepatic autoimmune disease (%)	Specific associated disease	(%)
Floreani et al. ⁵ / 2015/Italy	221	61	- Sjögren's syndrome	56
			- Raynaud's phenomenon	29
			- Hashimoto's thyroiditis/Graves' disease	24
Watts et al. ⁶ /2004/United Kingdom	160	53	- Sjögren's syndrome	25
			- Autoimmune thyroid disease	23
			- Rheumatoid arthritis	13
Wang et al. ⁷ /2013/ China	322	47	- Sjögren's syndrome	36
			- Systemic lupus erythematosus	4
			- Polymyositis	3
Gershwin et al. ⁸ /2005/USA	1,032	32	- Raynaud's phenomenon	12
			- Sjögren's syndrome	10
			- Rheumatoid arthritis	10
Mantaka et al. ⁹ /2012/ Greece	111	37	- Hashimoto's thyroiditis	18
			- Raynaud's phenomenon	6
			- Sjögren's syndrome	5
González-Huezo et al. ³ /2018/Mexico	78	63	- Sjögren's syndrome	30
			- Hypothyroidism	27
			- Raynaud's phenomenon	14
			- CREST syndrome*	11
			- Rheumatoid arthritis	8
			- Vitiligo	6
			- Scleroderma	5

C: calcinosis; E: Esophageal dysfunction; R: Raynaud's phenomenon; S: sclerodactyly; T: telangiectasia.

from international cohorts that included thousands of patients with PBC and they appear to be more accurate (GLOBE and UK-PBC).¹²

First-line treatment for PBC is UDCA, and 70 to 80% of patients are considered responders after 6 to 12 months of treatment.¹ For decades, the only treatment for PBC was UDCA. The use of obeticholic acid was recently authorized for non-responder patients.¹³ In addition, the combination therapy of UDCA plus bezafibrate was reported to have a higher complete biochemical response rate, compared with UDCA plus placebo.¹⁴

Treatment response in Mexican patients diagnosed with PBC was not an aim of the study conducted by González-Huezo et al.³ Nevertheless, we believe that it is essential to carry out future studies to evaluate whether the response to UDCA in the Mexican population is similar to that of other cohorts. Such knowledge is essential, because patients that do not respond to treatment with UDCA are at a higher risk for developing cirrhosis, presenting with complications secondary to portal hypertension, requiring a liver transplantation, and for death related to liver failure. It will also be necessary in the future to know the risk factors associated with the lack of response to UDCA in Mexican patients and their response to second-line treatments, such as obeticholic acid and bezafibrate.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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