DILI caused by antineoplastic and biological agents in patients enrolled in the prospective Spanish and Latin American DILI registries.

Materials and Methods: Information from well-vetted DILI cases caused by antineoplastic and biological agents enrolled in the Spanish DILI Registry (n=38) and the LATINDILI Network (n=33) since their establishment in 2022 was retrieved. Demographics, clinical characteristics, laboratory findings and outcome were analyzed through descriptive statistics.

Results: Overall, DILI patients were aged 61±17 years, with Latin American patients slightly younger than Spanish cases (64 vs. 56; p=0.053) and were predominantly men (66%). Novel therapies such as Protein Kinase Inhibitors represented 14% of cases, while Immune Checkpoint Inhibitors caused 6% of DILI cases. Hepatocellular damage predominated (79%), while 12% had a cholestatic injury. Nearly 70% of patients developed jaundice, and 49% were hospitalized. Alanine and aspartate aminotransferase were highly increased (median values 13 and 11 times above the upper limit of normal (ULN), respectively), while alkaline phosphatase showed modest elevations (1.3 times ULN). Total bilirubin was elevated by a median of 3.7-fold ULN. Most of the patients coursed with a moderate injury (46%), and 15% developed severe liver damage. Four Spanish cases, and one from Latin America, had liver-related death (p=0.018). There were no chronic DILI cases, and 71% of patients resolved spontaneously.

Conclusions: DILI, due to antineoplastic and biological agents, was more common in men, caused a hepatocellular injury, and usually coursed as a moderate-to-severe liver injury. Latin American cases were slightly younger, while the mortality rate was higher among Spanish DILI patients.

https://doi.org/10.1016/j.aohep.2023.101046

O-40 PROGNOSTIC ROLE OF MAGNETIC RESONANCE OF THE ABDOMEN WITH INTRAVENOUS CONTRAST AND CHOLANGIORESONANCE IN PRIMARY SCLEROSING CHOLANGITIS: OUR EXPERIENCE

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Introduction and Objectives: Primary sclerosing cholangitis (PSC) is a progressive cholestatic liver disease leading to infectious complications, biliary cirrhosis, portal hypertension and the development of cholangiocarcinoma. Imaging is essential for diagnosis. MRI risk scoring systems, called Anali without/with gadolinium, are suggested to predict disease progression. This study aimed to evaluate the usefulness of Anali scores determined by MRI of the abdomen and cholangioMR to predict the prognosis of patients with PSC.

- Analyze interobserver variability of Anali scores.

Materials and Methods: Cohort retrospective study of patients diagnosed with PSC, with baseline and follow-up MRIs (2009 to 2020). The study was approved by the institution's Ethics Committee.

MRIs were reviewed by two radiologists and Anali scores were calculated: without gadolinium= (0-2 x intrahepatic bile duct dilatation) + (2 x hepatic dysmorphism) + (1 x portal hypertension) with a possible score of 0 to 5; with gadolinium = (1 x hepatic dysmorphism) + (1 x heterogeneity of hepatic parenchymal enhancement) with a possible score of 0 to 2.

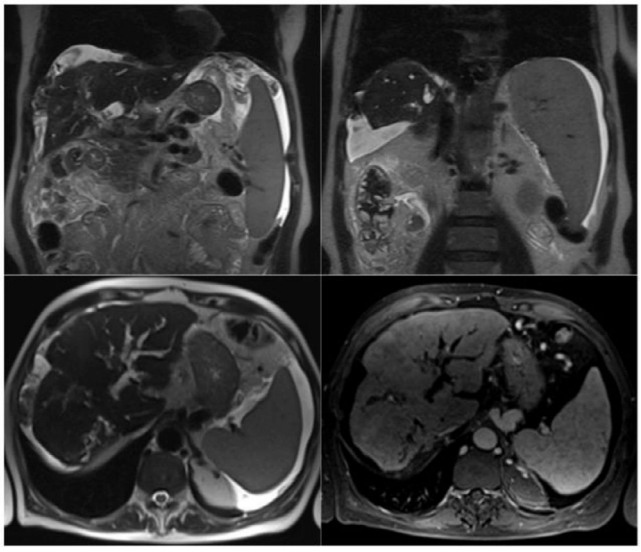
Clinical endpoints included liver transplantation, cirrhotic decompensation, or death.

Results: Twenty-nine patients were included, of whom 12 presented a clinical event on follow-up. We recorded seven liver transplants and five cirrhotic decompensations. The median time between the clinical event and MRI was 30.5 months.

Patients with a clinical event had a median Anali score without gadolinium 4 and with gadolinium 2, while in those without clinical events, the Anali score was 1 in both modalities.

The Kappa index for interobserver agreement with respect to the Anali score was 0.87 (95% CI). Kaplan-Meier survival analysis comparing event-free time according to the Anali scale was 59 months for scales 0-2 and 32 months for scales 3-5.

Conclusions: MRI Anali scores correlate with the occurrence of clinical events in PSC, with a high degree of interobserver agreement. They should be considered a useful prognostic tool in evaluating these patients.



https://doi.org/10.1016/j.aohep.2023.101047

O-41 CIRRHOSIS IN PATIENTS WITH ALFA 1 ANTITRYPSIN DEFICIENCY; WHAT ARE WE MISSING?

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Introduction and Objectives: It's common to include alfa 1 antitrypsin deficiency (AATD) in the diagnostic workup of children with cirrhosis, unlike in adults, where we seldom test for it. Some of its characteristics are unusual and we can miss them as it tends to have a silent clinical course, showing advanced indirect signs due to portal hypertension. This study aimed to establishing the biochemical, clinical, molecular, and genetic characteristics that can lead to the diagnosis of cirrhosis due to ATTD.

Materials and Methods: We analyzed 26 cases of adults with AATD related disease in Costa Rica. We establish presentation based on age, gender, AAT levels, phenotype genetic characteristics and clinical, biochemical and histological features.

Results: 26 patients had either hepatic or pulmonary chronic diseases in relation to AAT enzyme alterations, The proportion by sex was 1:1 and the mean age of diagnosis was 42. Of 21 patients with phenotyping, 9 were homozygous PI*ZZ (7) or PI: NullNull (2). Only this last group had the pulmonary disease. The ones homozygous for the PI*ZZ mutation all developed hepatic disease. Nonetheless, we also found that seven were heterozygous for PI*MNull, 4 for PI*MZ and 1 was PI*SZ. ATT levels were measured in 20 patients, 20% of them had normal levels and 15% were nondetectable. When a biopsy was obtained, the PAS staining was positive in 100% of cases. Several patients had liver steatosis instead of cirrhosis which was handled as NASH due to the similarity in clinical characteristics.

Conclusions: AATD can't only be screened through AAT levels as they can be normal in up to 20% of patients. We should establish the phenotype and keep in mind that heterozygous can develop clinical disease. The association with other forms of liver disease, especially such as MAFLD, is high and so we should screen for AATD in search of possible decompensation.

https://doi.org/10.1016/j.aohep.2023.101048

O-42 COSTA RICA NATIONAL NEWBORN SCREENING LABORATORYS EXPERIENCE IN DIAGNOSING ALPHA-1 ANTITRYPSIN DEFICIENCY

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Introduction and Objectives: Alpha-1 antitrypsin (AAT) is an acute-phase glycoprotein encoded by the *SERPINA1* gene. This allele has a codominant expression and Alpha-1 antitrypsin deficiency (AATD) is caused by the inheritance of two affected alleles. The spectrum of the disease depends on the variants and environmental and biological factors. This study aimed to divulge Costa Rica's experience in diagnosing AATD using biochemical and molecular approaches in patients referred to this center between 2014 and 2021.

Materials and Methods: : Forty-three patients (20 males and 23 females) were analyzed.

Biochemical parameters: Serum AAT concentrations were quantified by turbidometry (SPIN200E, ®SPINREACT). Protein electrophoresis and phenotyping isoelectric electrophoresis were performed on the HYDRASYS 2 SCAN FOCUSING (SEBIA).

Genetic characterization: Sanger sequencing of the *SERPINA1* coding regions (NM_000295.5) was performed in 16 patients with rare electrophoretic patterns or MM phenotype with low AAT concentration.

Results: In 43 probands, we found an AAT mean value of 60.7mg/dl and eight different electrophoretic patterns. Most of our affected patients had an MZ or ZZ phenotype. Table 1 shows the main phenotypes and genotypes of our patients (N=25 patients); how some of them share the same electrophoretic pattern; and finally, the correlation between clinical severity and the biochemical phenotype. Our lab found two variants, one related to null phenotype and the other with uncertain clinical significance (VUS).

Conclusions: :

- This laboratory has developed an efficient and comprehensive algorithm diagnosis for AATD that involves biochemical and molecular tools.
- Genetic analysis has allowed the identification of null variants (Q0Cork and Q0Lisbon).
- AATD affects children and adults, with a broad severity spectrum and different clinical presentations.
- Patients with one affected allele (e.g., PI*MZ, Pi*MS) might show some clinical manifestations.
- Accurate diagnosis is essential for optimal clinical attention and to reduce the diagnostic odyssey.

Table 1. Description of main probands phenotypes and genotypes in 25 of our patients

	AAT concentration (mg/dl)	Electrophoretic Pattern (by SEBIA)	Phenotype	* Genotype	
				Allele 1	Allele 2
Severe	0	Null	PI*Q0Q0	c.611_612delCA	c.611_612delCA
	27, 42, 23, 18, 25, 30, 24, 20, 8	ZZ	PI*ZZ	N/A	
	43	MZ	PI*M3Z	c.1096G>A p.(Glu366Lys) on M1A	WT
	62		PI*M3Z	c.1096G>A p.(Glu366Lys) on M1A	WT
	48		PI*M4Z	c.1096G>A p.(Glu366Lys) on M1A	WT
	69		PI*M1Z	c.1096G>A p.(Glu366Lys) on M1A	WT
	58		PI*M1Z	c.1096G>A p.(Glu366Lys) on M1A	WT
	88		PI*M1Z Augsburg	c.1096G>A p.(Glu366Lys) on M2	WT
	64	M/Rare	N/A	VUS: c.38C>A , p.(Ala13Glu)	WT
	65	SS	PI*SS	c.863A>T , p.(Glu288Val) on M1V	c.863A>T , p.(Glu288Val) on M1V
	70	M/Null	PI*M3Q0Lisbon	c.275C>T p.(Thr92Ile) on M1	WT
	81	MS	PI*M3T	c.863A>T , p.(Glu288Val) on M3	WT
	84	N/A	PI*M3S	c.863A>T , p.(Glu288Val) on M1V	WT
Normal	77, 166, 55, 49	MM	PI*M2M3, PI*M1M2, Pi*M1M1, Pi*M1M1	WT	WT

* Only in 16 patients genotype was analyzed
N/A: not analyzed.
WT: Wild type.

https://doi.org/10.1016/j.aohep.2023.101049

O-43 RISK FACTORS FOR CANCER DEVELOPMENT IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS

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