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.

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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.

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

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Introduction and Objectives: Primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH) and PBC overlap syndrome (AIH/PBC) have been associated with a higher risk of hepatocellular carcinoma (HCC) and extra-hepatic malignancy (EHM). This study aimed to assess potential risk factors associated with cancer development in PBC and AIH/PBC patients.

Materials and Methods: The Brazilian Cholestasis Study Group database was reviewed and analyzed.

Results: Among the 752 PBC patients enrolled, 64 of them with AIH/PBC, and 87 cancers were identified in 79 patients, including 20 cases of HCC and 67 of EHM. Patients with HCC had a higher prevalence of cirrhosis (95% vs. 32.5%, p= <0.001), smoking (55% vs. 12.3%, p= <0.001, CREST syndrome (30% vs. 7.6%, p= 0.003) and prior azathioprine (30% vs. 8%, p= 0.005) and prednisone (35% vs. 14%, p= 0.018) previous use, compared with their counterparts. Patients with EHM had a higher prevalence of smoking (42.3% vs. 12.3%, p= <0.001), AMA positivity (96.6% vs 80.6%, p = <0.001), azathioprine use (21% vs 8%, p= 0.01) and concurrent other autoimmune diseases. In multivariate analysis, cirrhosis, obesity and prior azathioprine therapy were independent risk factors for HCC, while Sjogren syndrome and psoriasis were associated with EHM. Fibrates reduced EHM risk.

Conclusions: The prevalence of EHM is higher when compared to HCC in PBC patients. Cirrhosis, obesity, prior azathioprine use, and concurrent autoimmune diseases were significantly associated with cancer in PBC, while fibrate use was apparently protective against EHM.

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OP-2 PREVALENCE OF NON-ALCOHOLIC FATTY LIVER DISEASE AND ITS ASSOCIATION WITH PHYSICAL ACTIVITY LEVELS AMONG ADULTS IN CHILE

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Introduction and Objectives: Non-alcoholic fatty liver disease (NAFLD) diagnosis requires a liver biopsy, which is inapplicable to large populations. Alternatively, NAFLD can be detected indirectly by non-invasive methods such as Fatty Liver Index (FLI) and Lipid Accumulation Product (LAP). Thus, the prevalence of NAFLD and its association with lifestyle habits (e.g., physical activity) can be studied within populations. This study aimed to (i) estimate the prevalence of NAFLD by FLI and LAP in the adult Chilean population and (ii) determine the association between the presence of NAFLD and physical activity levels.

Materials and Methods: We analyzed the National Health Survey of Chile 2016-2017. Individuals meeting these criteria were included: 21-75 years old; absence of hepatitis B/C, HIV, acquired immunodeficiency syndrome, syphilis, chancre, and gonorrhea; alcohol consumption <20 g/day for women, or <30 g/day for men. NAFLD was detected by FLI (considers circulating triglycerides, circulating gamma-glutamyl-transferase, body mass index, and waist circumference) and LAP (considers circulating triglycerides, and waist circumference). The Global Physical Activity Questionnaire was used to estimate physical activity levels. Logistic regression was used to determine the association between NAFLD presence and physical activity, adjusted by age, sex, body mass index, and education.

Results: We included 2,774 participants, representative of 10,599,094 [9,831,644−11,366,544] adults. NAFLD prevalence [95%CI] was 39.4% [36.2−42.8] by FLI, and 27.2% [24.2−30.4] by LAP. Prevalence progressively increased with higher body mass indexes. Compared to participants in the 1st-quartile of physical activity, those in the 3rd-quartile or 4th-quartile had lower odds of having NAFLD by FLI or LAP, respectively.

Conclusions: The prevalence of NAFLD in Chile surpasses global estimates. The excess body weight among adults in Chile may explain this phenomenon. Notably, physical activity seems relevant to prevent NAFLD, independently of excess body weight. Focused public health interventions are urgently required in Chile.

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