# The Color of Bile, PBC and AIH in Minority Women

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• I have nothing to disclose.

### PBC and AIH: A Strong Female Predominance

#### PBC

- 9:1 ratio F:M historic
- 4:1 ratio F:M modern
- Not a disease of children (role of hormones?)
- Genetic and environment interplay (UTIs? Xenobiotic theory).
- Traditionally (mistakenly) was thought to be a disease of White Europeans
  - Northern England, Australia etc

### AIH

- 3.6:1 ratio F:M
- Can present in children
- Genetic predisposition multiple HLA subtypes: DR3, DR4 etc
- Environment interplay (xenobiotics).
- Recognized in all races early on:
  - Recent recognition of disparities & varying severity and outcomes based on race/ethnicity.

Lu et al. *Clin Gastroenterol Hepatol.* 2018 Aug;16(8):1333-1341.e6; Kaplan et al. *Lancet.* 2004;363(9408):505; Mack et al. *Hepatology.* 2020 Aug;72(2):671-722.

# Prevalence of AILD is Increasing

#### PBC

- Until the 2010s, almost exclusively reported in Europe, Nort America, Australia, NZ → 10-22/100,000
- Previously reported as rare in Asia
- Since 2020 Asian countries reported PBC 4.7 South Korea, 5.6 Hong Kong and 49 per 100,000 in Southern China
- In Japan PBC tripled from 11.6 in 2004 to 33.8 per 100,00 in 2016
- US FOLD Study data prevalence of PBC (2003-2014)
  - 29/100,000 White
  - 20/100,000 Black
  - 22/100,000 ASINP

### AIH

- Swedish study from 1998 10.7/100k
- Denmark 23.9/100k from 1994-2012
- US study from 2014-2019 reported prevalence of 31/100,000
  - 13% Black
  - 2% Asian
  - 1% Latinx
- Pediatric incidence lower 0.2-0.4/100k
- Reported high incidence of AlH in Alaska Native 43/100,000
- Increasing world-wide prevalence of AIH up 50% over past decade!

Tanaka et al. *CLD*. 2021 Jan 13;16(6):227-230; Tunio et al. *J Clin Gastroenterol*. 2021 Nov-Dec; 55(10): 903–910; Lu et al. *Clin Gastroenterol Hepatol*. 2018 Aug;16(8):1333-1341.e6; Mack et al. *Hepatology*. 2020 Aug;72(2):671-722.

### Autoimmune Disease Prevalence Increasing





Period 1 (1988–1991, blue), period 2 (1999–2004, yellow), and period 3 (2011–2012, red).

Dinse et al. GE Arthritis Rheum 2020 Jun;72(6):1026-1035; Miller et al. Curr Opin Immunol. 2023 Feb;80:102266.



# History of AIH

1947 Himsworth Subacute Hepatic Necrosis			Treatment trials 60s-80s 1964 MacKay (Au)	1973 Rizzetto (London, UK)		Modern era with ↑ awareness of disparities
1945 by Barker, Capps and			Azathioprine and prednisolone	1985 Alvarez and 1987		1993 IAIHG established
Hargraves 1948 Lupus Erythromatous L.E. Cell	3 1955 MacKa Autoimmune Complem ANA+Lupoid he	iy ent Fixation patitis	1967 Blumberg Au ag HBS Twotypes of CAH 1971 Cook Mulligan, Sherlock (UK)	1977 Freudenberg (Germany)	200 Bla	01 Lim (Georgia US) 51pts, 27 Black acks 85% cirrhotic vs 38% on 1st bx
Thought to be triggered by virus		Race of each gro had a Je	and social status. There were two patients of African descent—one is up—one was from the Sudan and the other from Jamaica. Three patien wish ancestry. The remainder were all of European origin ; five were Irisi	1980 MacKay (Au) HLA A1, B8 and DR3 2	2002 70	2002 Hurlburt (Alaska US) Alaskans and Inuit pts with AIH
		All socia two grou	al strata were represented, and they were evenly distributed between th ups.	10	Youn	ger age and more cholestatic features
			1965 MacKay	1981 Berg (Germany)	200 E	7 Verma (MD, US) 138pts, 37 Black Blacks more aggressive disease, cirrhosis, ALF, need for LT
Kunkle 1950 (N 12 pts 11F lgG T	∕, US) P 9-13	963 Holborow ANA+	Coined Autoimmune Hepatitis 1965 Popper Pathologic Description Piecemeal necrosis Plasma cell hepatitis	1984 Czaja Prednisone		2012 Wong (CA, US) 183 AlH Latinx highest cirrhosis
Waldenstrom 1 Hypergammaglob	950 196 ulinemia 13 pt 1 Cen	4 Reynolds s 12F ANA+ tral American		1987 Mans Germany)	2018	Lee 63pts, 10 Black, 39 Latinx, 19 API Increased odds of AIH
Zimmerman 1951 ( A male patient	C USA) 3 Mexican gG 4 Black	Mexican 4 Black		And-SLA		2018 Wen (CA, US) Latinos higher hospitalization for AlH
sub-massive hepa Lymphocytes and p	c necrosis asma cells	elfer B. Reynolds, m. Robert L. Pet	upoid Hepatitis D., F.A.C.P., HUGH A. EDMONDSON, M.D., F.A.C.P., FERS, M.D., and Allan Redekker, M.D. Low Awards. Colifornia	C		

### Minorities and AIH

- Minorities have a higher OR for the diagnosis of AIH after adjusting for age and sex.
- Blacks and Latinx patients have a higher rate of hospitalization for AIH relative to their census population.
- Alaskan Natives have a high prevalence of AIH 43/100,000 and more jaundice at presentation.
- Hispanics more commonly present with cirrhosis:

	Adjusted OR	95% CI	p-values
Race			
White	REF	REF	REF
Black	9.6	(1.8, 177.5)	0.03
Latino	25.0	(5.3, 448.3)	< .01
API	10.8	(2.2, 195.8)	0.02
Other	0.9	(0.0, 22.1)	0.92
Sex			
Male	REF	REF	REF
Female	5.8	(2.9, 13.4)	< .01
Age	1.0	(1.0, 1.0)	0.10

Our USC cohort 28% had  $\geq$ F3 at presentation, but 19% had PBC-AlH variant and among those 60% had advanced fibrosis at presentation.

•	Black	patients	with	AIH
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- Present at a younger age.
- Have more severe disease.
- More cirrhosis on index liver biopsy.
- Higher rates of liver failure, LT and death.
- The overall mortality in black patients (24.3% versus 6.2%, P 0.009).

Multivariable Model of Factors Associated with AIH Diagnosis

Lee et al. *Autoimmunity*. 2018 August ; 51(5): 258–264; Lee BT et al. *Hepatology*. 2021 Nov;74(5):2876-2887; Lee BT et al. *Hepatology*. 2017;66 (Suppl.1) : 149-1185; Thuluvath PJ et al. *Arch Med Sci*. 2015;11:1227-1235; Zolfino T et al. *Gut*. 2002;50:713-717; Verma Hepatology. 2007 Dec;46(6):1828-35; Lim et al. *Am J Gastroenterol*. 2001 Dec;96(12):3390-4. Chung HV et al. *Can J Gastroenterol*. 2007;21:565-568; Minuk GY et al. *Can J Gastroenterol*. 2008;22:829-834.



### History of PBC



### **Minorities and PBC**

- Latinx and Black patients are more likely to present with decompensated liver disease.
  - Black patients present younger.
    - Lower odds of receiving UDCA! Possible misdiagnosis?
  - Black pts higher odds of mortality (OR 1.34 95% CI 1.08-1.67) which reversible with UDCA.
  - Latinx pts more advanced disease, less responsive to UDCA, higher mortality.
  - Latinx pts more variant/overlap disease.
  - AAPI and AI high risk and LT and death, less UDCA use, least studied.
- All minorities have higher odd of hospitalization (OR 1.9 95% CI 1.7-2.1).
- Lower income, less insured, lower literacy level.
- Less liver transplant.
- Latinx pts higher MELD at LT and high waitlist mortality.
- All patients of color are under-represented in clinical trials.

Peters et al. *Hepatology*. 2007;46(3):769-75; Levy et al. *CGH*. 2014;12:1398-1405; Lu et al. *CGH*. 2018;16:1333-1342; Lu et al. CGH. 2018;16:1333-1341.e6; Galoosian et al. *Dig Dis Sci*. 2020;65(2):406-415; Sayiner et al. *Hepatology*. 2019;69(1):237-244; Cholankeril et al. *Clin Gastro Hepatol*. 2018;16(6):965-973; Adjemo et al. *Dig Dis Sci*. 2021;66:1461-1476; Rabiee et al. *J Clin Trans Hep*. 2020;8:391-396.

### **Raising Awareness**

- Misdiagnosis and under-diagnosis.
- UDCA improves LT-free survival.
  - − PBC median time to  $\ge$  F3  $\rightarrow$  2 years.
  - 50% of untreated PBC patients progress to cirrhosis by 4 years.
  - Cirrhosis at presentation worse prognosis for both AIH and PBC.
    - Early diagnosis and access to care and regular health maintenance.
- Etiology? Interplay of biology and environment including physical environment (toxic waste), social, and economic factors.

Mitchison et al. *Gastroenterology*. 1990;99:778-784; Kaplan et al. *NEJM*. 2005;353:1261-73; Christensen et al. *Gastroenterology*. 1985;89: 1084-1091; Corpechot et al. *Hepatology*. 2000;32:1196-1199; Prince et al. *Hepatology*. 2001;34(6):1083; Ala et al. *Hepatology*. 2006;43(3):525. Harms *JHep* 2019 Aug; 71(2):357-365.





Adapted from Lee BT et al. *Hepatology*. 2021 Nov;74(5):2876-2887

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# Work To Be Done in PBC and AIH

#### **Clinical Care**

- Cultural and linguistic competency of providers.
- ↑ Recruiting minority providers
- Educate providers about AIH and PBC in racial and ethnic minorities
- ↑ Telemedicine, ↑ access to hepatologist provider networks

#### Research

- Need biological data
- Study clinical outcomes systematically in minorities
- ↑ SDOH research
- Enroll minorities in RCTs
- Diversify research staff, use multilingual team (Spanish, Mandarin etc)
- Collaborate →rare disease

#### **Public Policy**

- ↑ Social workers
- ↑ Health coverage for indigent and immigrant patients
- ↑ Community health clinics, better access to specialty care (telehealth?)
- Access to screening (incidentally abnormal labs)
- Political advocacy

# Thank you!

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