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Background: Peripheral blood (PB) regulatory T cells (Tregs) in post-transplant alloimmune hepatitis (DAIH) & autoimmune hepatitis (AIH) have poor regulatory function, however little is known about intrahepatic (IH) Tregs in both diseases. As the human Treg compartment encompasses multiple subsets that delineate different developmental stages & their associated regulatory function, we used mass cytometry & unsupervised clustering algorithm Flow self-organizing map (FlowSOM) to interrogate the distribution of subsets within *ex-vivo* $CD25^{hi}CD127^{lo/neg}FoxP3^{+}$ Treg in PB & liver (IH) of children with DAIH & non-transplanted children with AIH. **Methods:** Enriched $CD4^{+}$ T cells from peripheral blood mononuclear cells (PBMC) and intrahepatic lymphocytes (IHL) of children with DAIH (n = 5), AIH (n = 5), biopsy proven acute rejection (AR) (n = 3), liver transplanted children with graft dysfunction (n = 6), & liver transplanted children with normal graft function (LTC) (n = 14) were expanded in culture with Dyna beads CD3/CD28, rIL-2 & TGF-b for 5-days prior to FACS sorting of Tregs. For FACS sorting, Tregs were identified by high expression of CD25 & low expression of CD127. *Ex-vivo* sorted PB & IH Tregs were then stained for mass cytometry with metal-conjugated monoclonal antibodies (CD49D, CD4, CCR4, CD45RA, CD3, CD39, FoxP3, CD95, CD45RO, CD25, CD152, HLA-DR, CD127, CD73, NRP1, Helios, LAP, CD45). Cells were acquired using a CyTOF Helios mass cytometer. CyTOF data was time-based bead normalized using standard procedures. The data were then uploaded to OMIQ (Omiq.ai), manually gated using Gaussian parameters to resolve live, intact, single cells for further analysis. Expression levels were arcsinh transformed with a cofactor of 5 and compared across disease groups within the Treg population. Clustering was performed using FlowSOM & visualized using dimensionality reduction using UMAP. All statistical analyses were performed in GraphPad Prism v9 (Dotmatics). **Results:** Demographics reported in Table 1 below. 10 phenotypically distinct clusters were identified based on15 analyzed parameters within PB & IH Tregs of DAIH, AIH patients, as well as LTC subjects. IH Tregs of AIH patients were characterized by a higher CD45RA, & lower CCR4, Helios, FoxP3, CD25, CD73, CD39, CD45RO, & CD95 expression when compared with PB Tregs ($p < 0.001$). IH Tregs of DAIH patients were characterized by a higher expression of CD45RA, CCR4, CD25, CD73, CD95, & lower expression of FoxP3, Helios, CD39 compared to PB Tregs ($p < 0.001$). An important suppressive mechanism mediated by Treg involves the CD39/CD73 adenosine pathway. In humans, $CD39^{+}$ Tregs are implicated in the suppression of Th17 responses & the control of autoimmunity. **Conclusion:** The lower expression of FoxP3 & Helios in IH Tregs of patients with DAIH & AIH could suggest Treg destabilization. Further work is needed to determine if these IH Tregs have the potential to transdifferentiate into effector T cells.

	Post-transplant alloimmune hepatitis (n=5)	Autoimmune Hepatitis (n=5)	LT Control (n=14)	Acute Rejection (n=3)	Graft Dysfunction (n=6)
Age at blood draw (years) Median (IQR)	16.8 (13.7-18.0)	10.7 (8.4-14.9)	5.9 (2.1-8.1)	1.9 (1.1-2.3)	7.0 (1.5-14.6)
Duration from transplant at blood draw (years) Median (IQR)	12.8 (11.0-18.2)	n/a	4.2 (1.0-5.4)	1.35 (1.34-1.8)	0.5 (0.2-0.8)
ALT at blood draw (U/L) Mean (SD)	108 (112)	195 (274)	21.6 (7.3)	299 (253)	212 (288)
Tacrolimus level at blood draw (ng/L) Mean (SD)	5.4 (2.9)	n/a	5.6 (3.7)	5.6 (8.1)	7.2 (1.5)
Sex (M/F)	2/3	3/2	10/4	2/1	1/5

Disclosures: The following people have nothing to disclose: Udeme Ekong
Disclosure information not available at the time of publication: Kumar Subramanian, Jhalen Ascue, Vinona Muralidaran, Nada A. Yazigi, Khalid M Khan, Bernadette E. Vitola, Stuart S. Kaufman, Alexander Kroemer, Thomas Fishbein, Eric Haas

134 | CENTER-SPECIFIC DATA FROM THE INTERNATIONAL MULTICENTER PEDIATRIC PORTAL HYPERTENSION REGISTRY (IMPPHR) – INITIAL ANALYSES OF 23 INTERNATIONAL SITES

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Symbols: ♦, Poster of Distinction; ★, Foundation Award Recipient

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Background: There are very limited high-quality data from which to derive therapeutic approaches to portal hypertension (PHT) in children. Management of varices, in particular, is quite controversial in pediatrics. IMPPHR was developed to derive large-scale international data, thereby enhancing our knowledge of PHT. The three major foci of data collection in IMPPHR are, 1) morbidity and mortality of first variceal hemorrhage, 2) feasibility and safety of primary prophylaxis of varices, 3) approaches to secondary prophylaxis of variceal hemorrhage. Subject level data collection is ongoing in IMPPHR (n = 241 cases as of 4.27.23) and will be reported in the future. This report provides center-specific data relevant to the management of varices. **Methods:** Each site submitted institutional resources and clinical activity accrued over 2 years between January 1, 2018 and December 31, 2019 to present a snapshot of resources and approaches available in clinical practice. **Results:** 23 centers (11 countries, 4 continents) serving an aggregate population of > 100,000,000 with 5970 hospital beds and 1024 ICU beds provided site specific data. Overall 600 liver transplants were performed at the sites for indications that included but were not limited to PHT ([median per center] 19: [25-75%ile] 6-34) of which 112 (1: 0-6) were living donor and 222 (5: 0-10) were technical variant grafts. In aggregate, 885 (23: 15-38) endoscopic variceal ligations were performed by 99 (4:2-6) individual's, while 266 (3:0–10) endoscopic sclerotherapy sessions were performed by 46 (2: 0-3) individual's. Potential two year endoscopic practitioner caseload varied significantly by site (variceal ligation 7: 2.8-13.8, sclerotherapy 1.5: 0.0-5.0). Nontransplant nonendoscopic interventions for PHT included 55 (range per center 1–20) portosystemic shunts (12/23 centers), 21 (range 1–5) TIPS (8/23 centers) and 30 (range 1–8) MesoRex bypass procedures (11/23 centers). 8 centers, Group A, performed at least 3 of at least one of these nontransplant nonendoscopic procedures; their center characteristics differed from the remaining 15 centers, Group B (Table). **Conclusion:** A multi-center registry focused on pediatric esophageal varices, has been developed with ongoing patient data entry. Site specific data reveals marked variability in approaches. Many pediatric centers perform only small numbers of endoscopic procedures for PHT, often divided among several proceduralists. There is also variable and limited use of nonendoscopic nontransplant interventions for PHT. IMPPHR will permit analysis of the impact of differences in approach on outcomes, helping to inform optimal treatment decisions and program planning. Supported by the Spain Family and an ESPGHAN Networking Grant.

Characteristic ->	Population of area (M)	Hospital Beds	OLT	LRD	Tech Variant	EVL	EST
Group A (n = 8)	7.3 ± 4.8	259 ± 168	38.5 ± 34.0	7.2 ± 6.9	20.5 ± 29.4	65.8 ± 68.7	22.6 ± 25.2
Group B (n = 15)	2.8 ± 2.7	259 ± 130	19.5 ± 22.0	3.6 ± 7.5	3.9 + 4.8	23.9 ± 14.0	5.7 ± 11.9
p-value	0.009	1.000	0.118	0.273	0.041	0.031	0.039

Group A – at least 3 MesoRex Bypass, Portosystemic Shunt or TIPS, Group B – the rest
* mean ± standard deviation, M = million, OLT = orthotopic liver transplant, LRD = living related donor, Tech variant = technical variant graft, EVL = endoscopic variceal ligation, EST = endoscopic sclerotherapy

Disclosures: Tassos Grammatikopoulos – Albireo and AstraZeneca: Consultant, No, No;
Samar H. Ibrahim – Alberio Pharam: Consultant, No, No; Mirum pharmaceutical: Consultant, No, No;
Amal A. Aqul – Mirum Pharmaceuticals, Inc: Consultant, Yes, No; Albireo: Consultant, No, No; Sarepta Therapeutics: Consultant, No, No;
The following people have nothing to disclose: Eyal Shteyer, Sara Hassan, Mercedes Martinez, Benjamin L. Shneider
Disclosure information not available at the time of publication: Simon C. Ling, Jean Pappas Molleston, Catalina Jaramillo, Julio Rocha Pimenta, Rustam Yuldashev, Sakil Kulkarni, Pooja Reddy Spector, Amy Feldman, Mohit Kehar, Voytek Slowik, Kee Seang Chew, Anja Praprotnik Novak, Scott Elisofon, Alexis Gumm, Anita K Pai, Juan Cristóbal Gana, Rodrigo Vazquez Frias, Oanez Ackermann, Mathieu Duche, Chaitri Desai, Matjaz Homan, Katherine Sweeny, Saima Deen, Serpil Tutan, Uma Ramamurthy, Riccardo A. Superina, Jaime Bosch, Roberto De Franchis

135 | PNPLA3 GENOTYPES ARE SIGNIFICANTLY ASSOCIATED WITH LIVER-RELATED OUTCOMES IN INDIVIDUALS WITH BIOPSY-PROVEN NONALCOHOLIC FATTY LIVER DISEASE (NAFLD)

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