

HDV diagnosis and treatment in Pakistan and the way forward for LMICs

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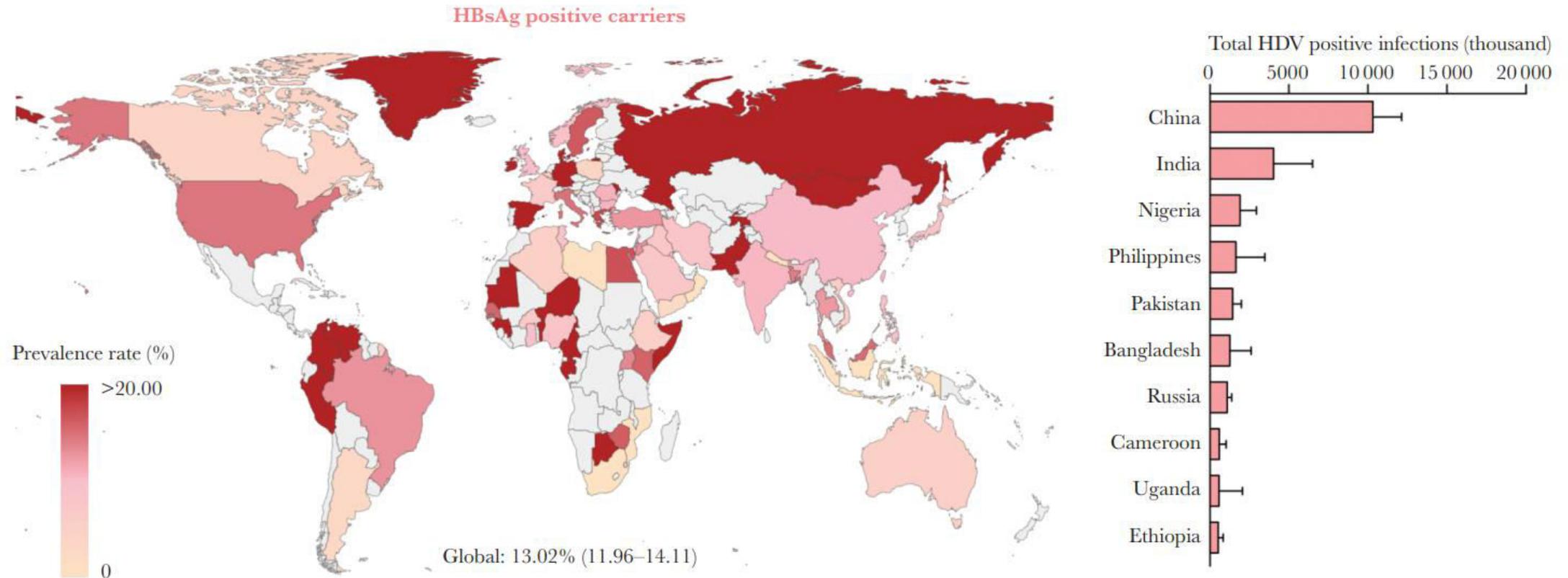
Karachi, Pakistan.

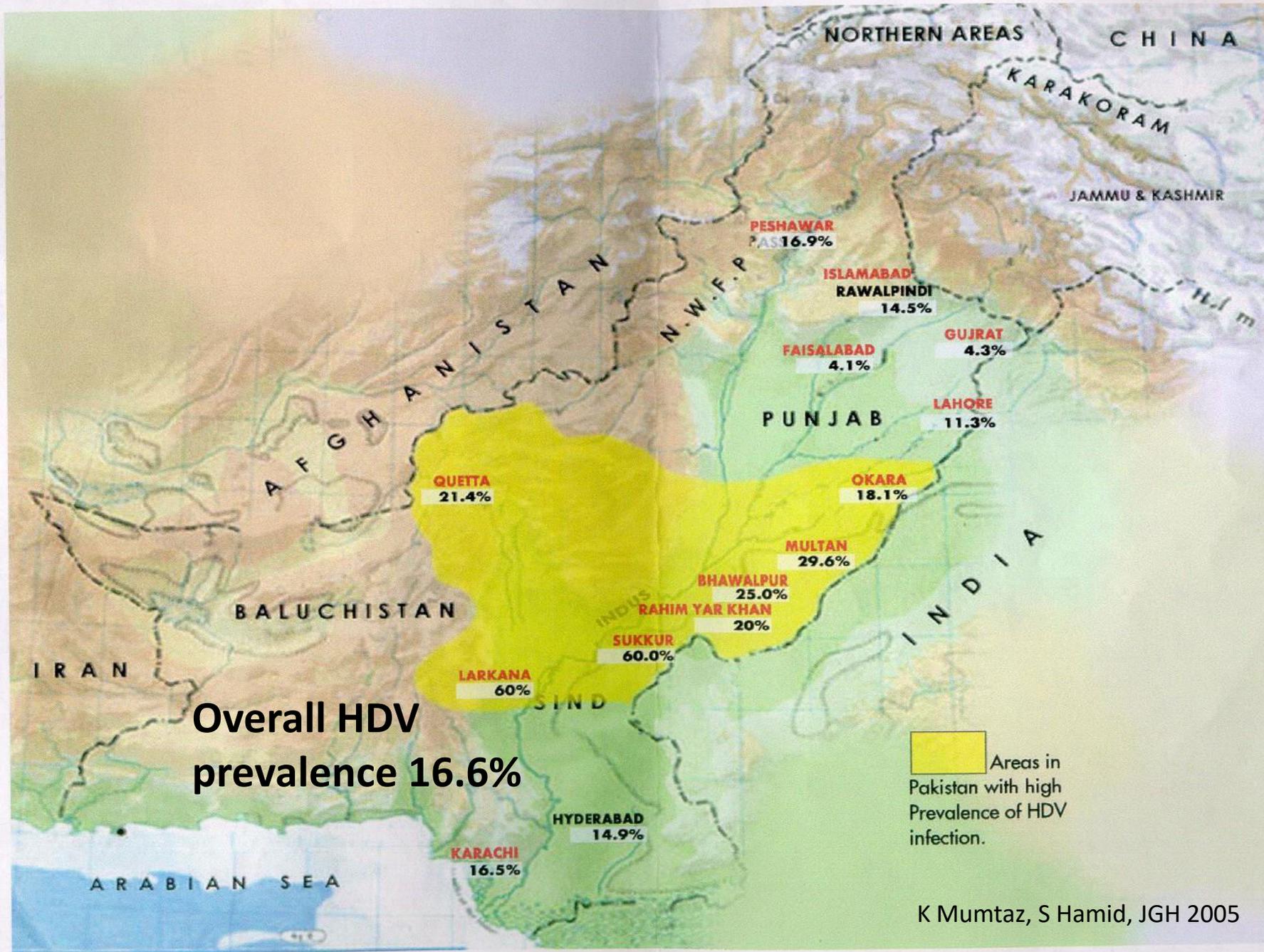


Disclosures

- Research funding from Abbott, Roche and Gilead.

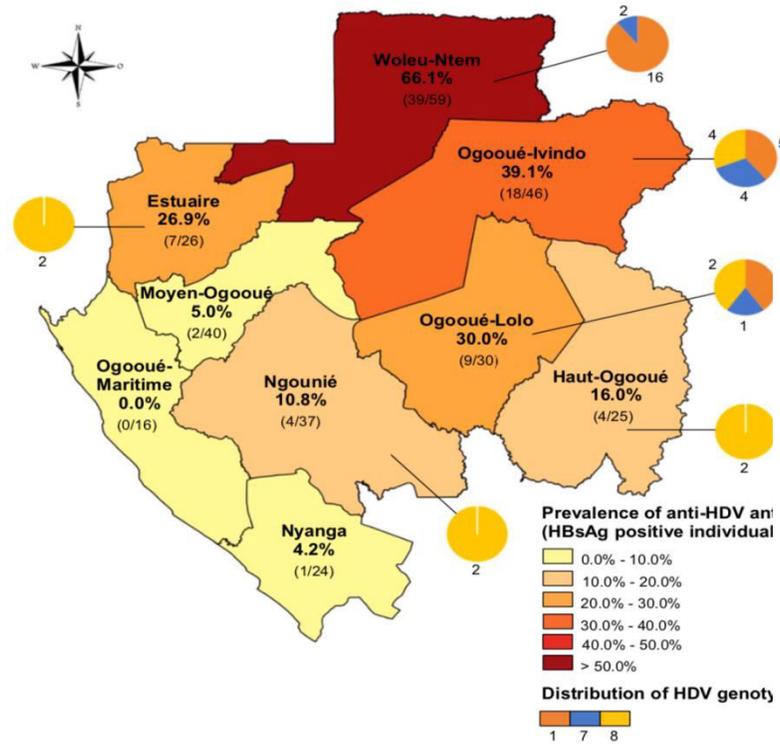
Global prevalence of HDV infection (HBsAg Carriers)





REGIONAL PREVALENCES OF ANTI-HD IN HBsAG POS.

Gabon Groc S, J Viral Hepat 2019; 26:170.

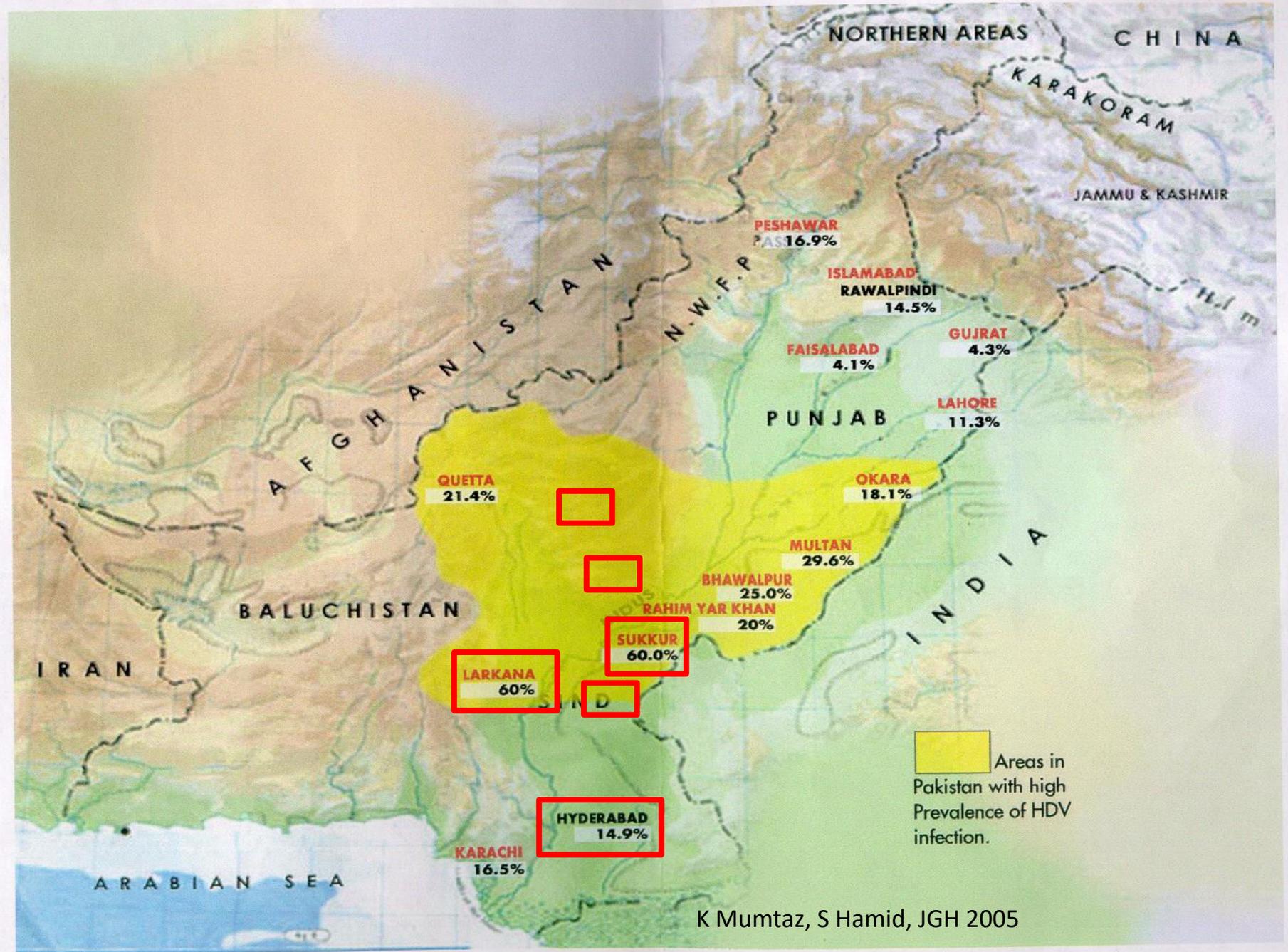


Burkina Faso

Tuailleon E, Lancet Glob Health. 2018;6(1):e33.



11 Sentinal sites
opened up by Sindh
Govt for HDV diagnosis
and treatment,
Starting in 2010





HEPATITIS CONTROL PROGRAM (CDC-II)

DELTA PATIENTS REPORT



| S/no. | SENTINEL SITE NAME | DISTRICT | WAITING PATIENTS | UNDER TREATMENT PATIENTS | COMPLETED CASES | DEFUALTER CASES | TOTAL no.OF PATIENTS REGISTERED UNDER TREATMENT/COMPLETED /DEFUALTER |
|--------------------|---|---------------------|------------------|--------------------------|-----------------|-----------------|--|
| 1 | Sindh Government Hospital Qasimabad Hyderabad | HYDERABAD | 0 | 69 | 115 | 38 | 222 |
| | | THATTA | 0 | 0 | 0 | 0 | 0 |
| | | KARACHI | 0 | 0 | 0 | 0 | 0 |
| | | SUJAWAL | 0 | 0 | 0 | 0 | 0 |
| | | JAMSHORO | 0 | 0 | 0 | 0 | 0 |
| | | BADIN | 0 | 0 | 0 | 0 | 0 |
| | | MATLI | 0 | 0 | 0 | 0 | 0 |
| 2 | DHQ hospital Tando Alahyar | TANDO ALLAHYAR | 0 | 8 | 37 | 4 | 49 |
| 3 | Civil hospital Mirpurkhas | MIRPURKHAS | 0 | 5 | 46 | 3 | 54 |
| | | UMER KOT | 0 | 12 | 38 | 1 | 51 |
| | | MITHI | 0 | 0 | 3 | 0 | 3 |
| 4 | Civil hospital Shaheed benazirabad | SHAHEED BENAZIRABAD | 0 | 59 | 192 | 9 | 260 |
| | | NOSHEHRO FEROZE | 0 | 60 | 80 | 9 | 149 |
| | | SANGHAR | 0 | 111 | 109 | 8 | 228 |
| 5 | KMC (Civil Hospital Khairpur) | KHAIRPUR MIRS | 0 | 90 | 212 | 17 | 319 |
| | | KINGRI | 0 | 0 | 0 | 0 | 0 |
| | | SOBODERO | 0 | 0 | 0 | 0 | 0 |
| | | KOT DIJI | 0 | 0 | 0 | 0 | 0 |
| | | THARI MIR WAH | 0 | 0 | 0 | 0 | 0 |
| 6 | GMMMC (Civil Hospital Sukkur) | SUKKUR | 0 | 237 | 166 | 85 | 488 |
| | | SHIKARPUR | 0 | 0 | 0 | 0 | 0 |
| | | GHOTKI | 0 | 0 | 0 | 0 | 0 |
| 7 | Civil hospital Larkana | LARKANA | 0 | 242 | 265 | 0 | 507 |
| | | KAMBER@SHAHADAD KOT | 0 | 0 | 0 | 0 | 0 |
| 8 | JIMS Institute Jacobabad | JACOBABAD | 0 | 57 | 200 | 58 | 315 |
| | | KANDHKOT@KASHMORE | 0 | 0 | 0 | 0 | 0 |
| 9 | Civil Hospital Dadu | DADU | 0 | 30 | 49 | 12 | 91 |
| 10 | Taluka Hospital Hala | HALA | 0 | 16 | 30 | 1 | 47 |
| 11 | Gambat (GIMS) Hospital | (GIMS) GAMBAT | 0 | 267 | 172 | 91 | 530 |
| GRAND TOTAL | | | 0 | 1263 | 1714 | 336 | 3313 |

HDV Data Analysis of Sukkur Sentinal site

- **Study site:**

GMM Medical College Hospital, Sukkur, which is the regional referral center for HDV patients.

- **Study Design:**

Cross Sectional Study of all patients presenting for treatment between August 2010 and June 2015.

- **Inclusion Criteria:**

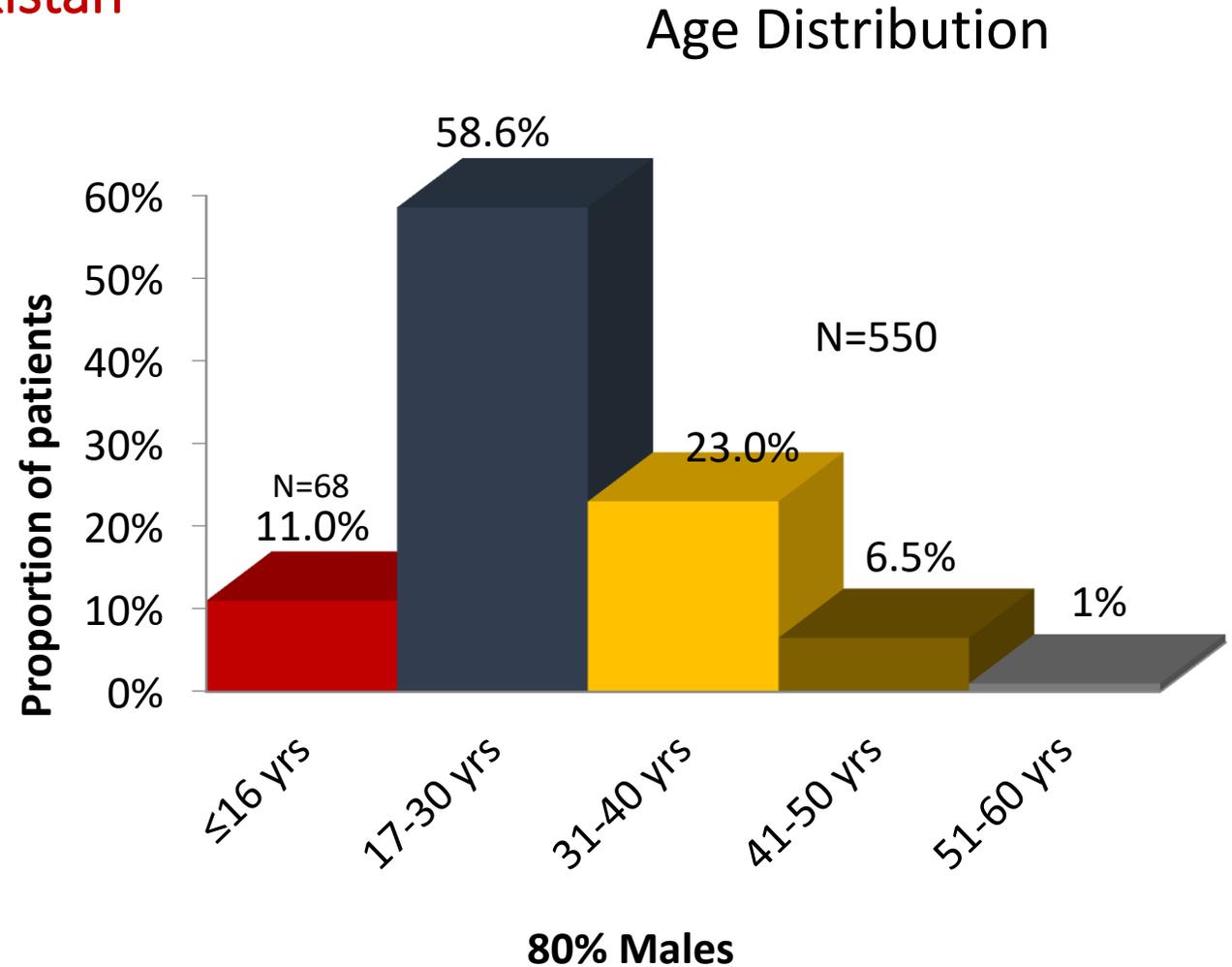
All compensated HDV + (Antibody and PCR) patients who had a liver biopsy as part of the treatment protocol.

- **Exclusions:**

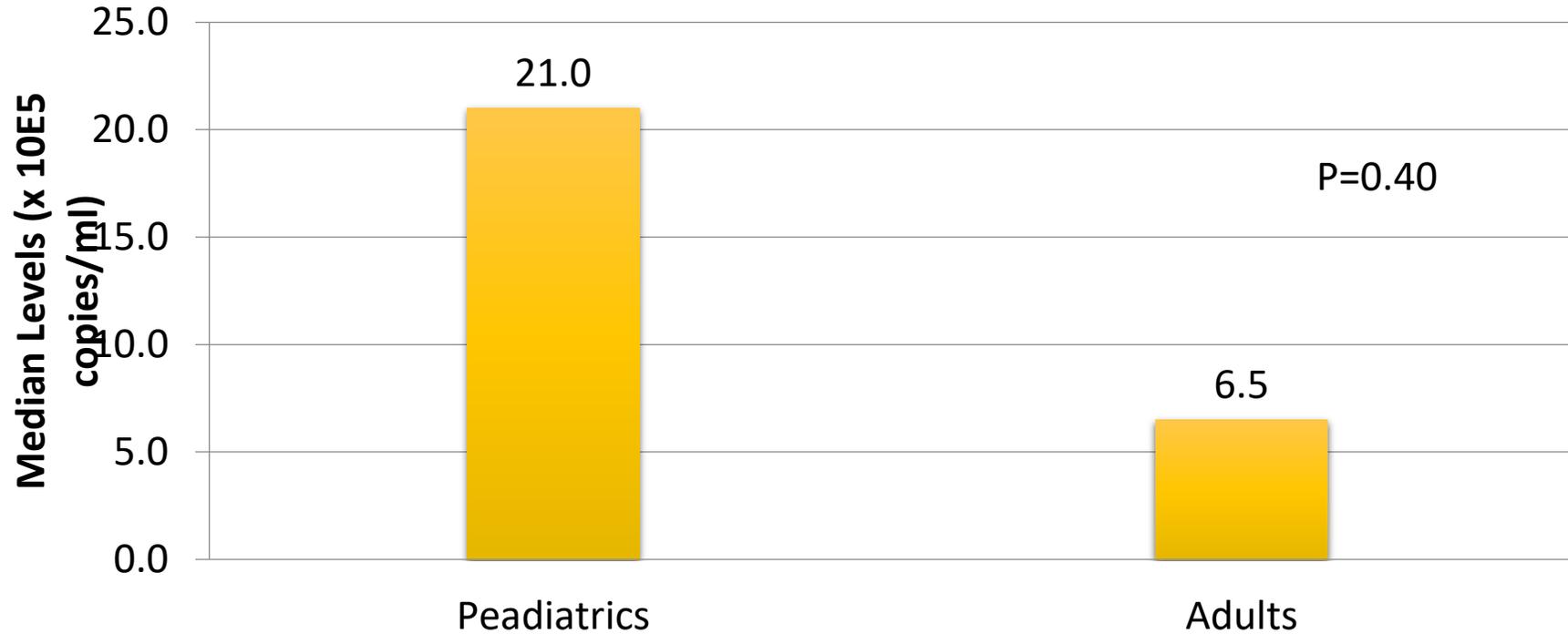
Patients with decompensated liver disease, were HDV antibody+ but HDV RNA – , or were triply infected with HBV/HDV/HCV.

HDV in Children and Adolescents in Pakistan

- Cross Sectional Study of all patients (N=618) presenting for treatment between 2010 and 2015, at regional referral center, Sukkur.
- All compensated HDV + (Antibody and PCR) patients had a liver biopsy as part of the treatment protocol.
- Overall 338 patients (54.7%) had severe fibrosis (stage 3 and 4).
- A higher proportion of pediatric patients had severe fibrosis as compared to adults (73.8 % vs. 57.2 %, p=0.01).

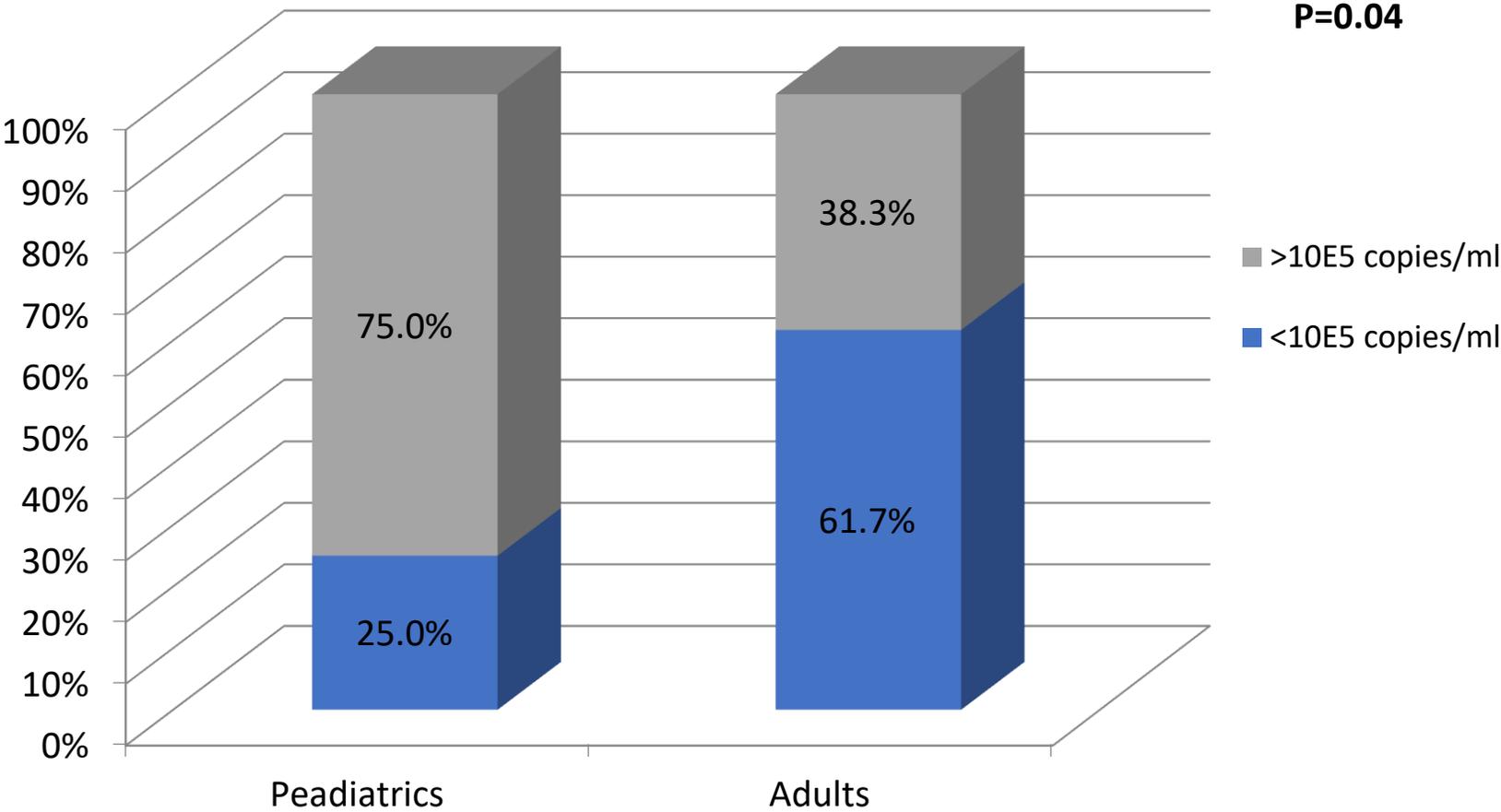


Quantitative levels of HDV RNA by age groups



| | Pediatrics | Adults |
|-----------------------------|---|--|
| HDV RNA levels, median(IQR) | 21 x10 ⁵ (1.7 x 10 ⁵ to 7.4 x 10 ⁶) | 6.5 x 10 ⁵ (7.1 x 10 ⁴ to 4.4x 10 ⁶) |

HBV DNA copies/ml according to age groups



* HBV DNA was negative in 11% of pediatric patients and 23.5% of adult patients

LDLT at Gambat/Sukkur for Viral Hepatitis (2016- March 2022)

| Etiology | # | % |
|-----------------|----------|----------|
| HBV | 121 | 25 |
| HCV | 161 | 33.5 |
| HBC+ HCV | 12 | 2.5 |
| HDV | 188 | 39 |
| Total | 482 | |

HDV: Pakistan vs rest of the World

- Patients from Eastern Europe (35.7 years; range:1-79) and Pakistan (32.7 years; range: 11-70) were **younger** (both $P < .01$).
- Patients from Pakistan were more **likely to be HBeAg positive** (35.2%) compared to patients from other regions (10.3%-16.1%).
- **HDVRNA was found to be more often positive** in patients from Pakistan (86.9%) and Eastern Europe (86.4%) (CE 58.9%, SA 46.1%).
- In Pakistan 60.8% of the patients were **HBV DNA positive** compared to 14.0% in South America ($P < .01$)

Diagnostic Modalities currently Available in Pakistan

- HDV Antibody: Diasorin SPA performed on ET-Max 3000 by ELISA
- HBV DNA Quantitation : COBAS AmpliPrep/COBAS TaqMan HBV Test.
- HDV RNA Quantitation : Analytik Jena Real time PCR Robogene 2.0

Cobas HDV has recently become available for Research Use Only

The Aga Khan University central lab is CAP accredited

The current treatment situation

- Peg-IFN not available since many months due to disruption in supplies.
- Bulevertide: Not registered

Patient access programs have not yet started.

Patient participation and Retention in HDV Clinical Trials

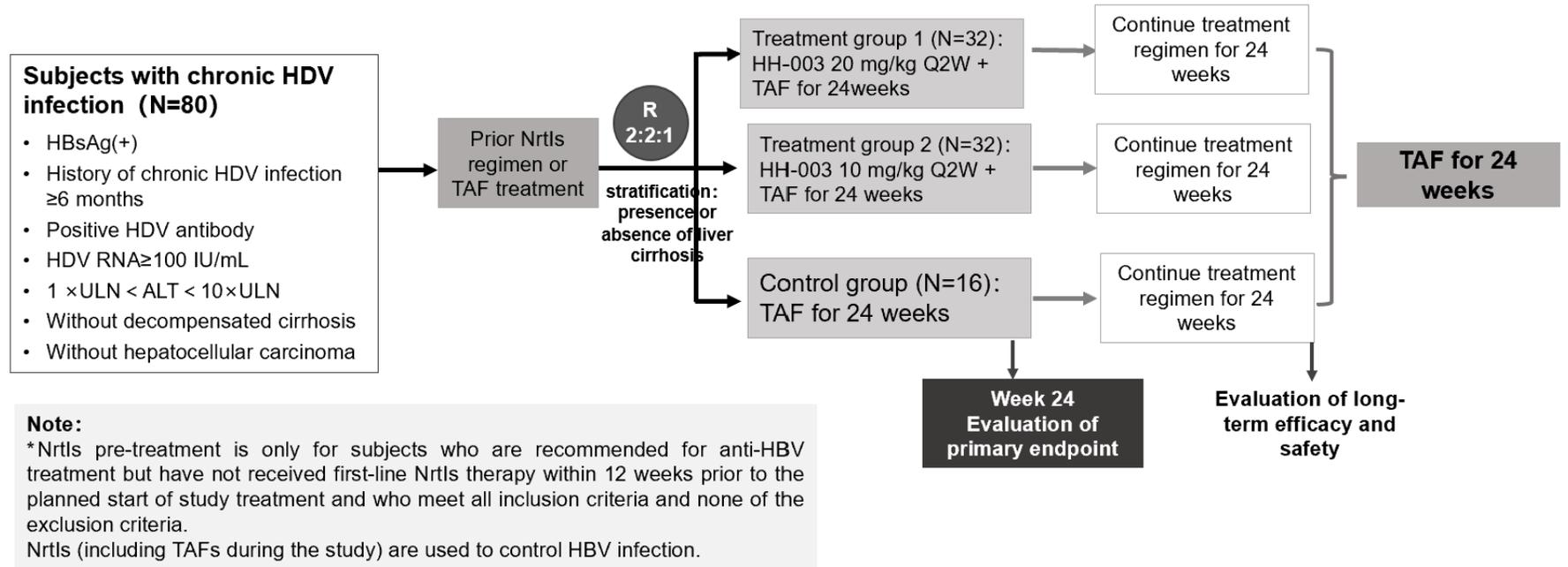
| Trial | IP | Patients Enrolled | Patient Compliance to Protocol | Outcomes |
|--------------------|--------------------------------|-------------------|--------------------------------|---|
| Limit-1 Phase 2 | PEG IFN Lambda | 15/33 | 100% | 36% DVR at EoFU (Wk 72) |
| D-LIVR Phase 3 | Lonafarnib ± PEG-Interferon | 53/402 | 3/53 (94%) | 24.6% composite end point wk 72 ≥ 2 HAI improvement |
| HH-204 Phase 2 | HH-003 | 45/60 | 100% | |

Study Design

- Multicenter, randomized, controlled, open-label Phase IIb clinical study to evaluate the **efficacy** and **safety** of HH-003 in subjects with **chronic HDV infection**.
- Planned to enroll **45** eligible subjects from ex-China countries with chronic HDV infection.



- 3 stages:
 - Screening period (up to 4 weeks)
 - NrtIs Pre-treatment period (up to 12 weeks), treatment period (24 weeks+24 weeks)
 - Follow-up period (24 weeks)



To Conclude.....

- HDV is a public health issue of major concern in Pakistan, and many other LMICs.
- Improvement in diagnostics is urgently needed to accurately define epidemiology
 - A dual RDT for HBsAg and HDV Ab
 - More choices for HDV RNA PCR testing- cobas HDV (RUO)
- Availability of Peg-IFN, specially in the absence of other therapies, is required.
- Patients in Pakistan, and other LMICs, stand to benefit from international clinical trials.
- Presence of international CROs, such as IQVIA, in the country has helped.