6th International Workshop on HIV Pediatrics

Abstracts
Oral presentations

Abstract: O_01

HIV antibody detection in children who started antiretroviral treatment in infancy

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Background: Negative results on standard HIV antibody (Ab) tests have been described among HIV-infected children initiating antiretroviral therapy (ART) early in life and remaining suppressed on ART. The Mississippi baby, who started ART <30 hours of birth and who maintained viral control after ART was stopped, also had negative HIV Ab results. The frequency of this phenomenon in clinical populations is unknown.

Methods: We selected 104 samples from HIV-infected children enrolled in one of our clinical trials in Johannesburg, South Africa. We chose samples from children who were suppressed (<50 cpm), had received ART for a mean of 5 years (range 3.4–6.4 years) and who started ART <15 months of age - mean age at ART start 8 months (range 2.2-15 months). We tested all children using a standard ELISA (Genescreen™ HIV1/2 version 2; Bio-rad) and all children with negative or low values were re-tested using the Sedia™ HIV-1 Lag-Avidity EIA (Sedia Biosciences).

Results: Of 104 children tested, 5 had undetectable Ab (neg) and 2 had low Ab reactivity (low). All of the children with neg/low were <6 months of age at ART start (mean 3.7 months, range 2.2 to 4.9 months). Overall 7/43 (16%) children <6 months at ART start had neg/low Ab. Duration of ART was not associated with Ab detection. Optical density (Ab ~quantity) was significantly lower among children starting ART <6 months of age, mean 3.6 OD, than those starting ≥ 6 months, 4.7 OD units, p=0.0002. When re-tested with the more sensitive assay 7/7 children with neg/low Ab tested positive.

Conclusions: The prevalence of HIV Ab negativity, even among children initiating ART <6 months of age, was lower than expected, and all had detectable Ab on a sensitive, low avidity assay. We hypothesize that children started ART too late (youngest age 2.2 months) for the majority to become HIV Ab negative. Nevertheless, the unusual Ab profiles suggest that early ART may have influenced the ontogeny of Ab responses. Further investigation of Ab development, early treatment and establishment of viral reservoirs is warranted.

No conflict of interest

Abstract: O_02

Performance of Dried Blood Spot specimens prepared under field conditions to identify virologic failure among Kenyan children on antiretroviral therapy

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Background: Viral load (VL) is recommended by WHO for monitoring antiretroviral treatment (ART) and determining virological failure (VF) in HIV-infected persons, but costly and stringent cold chain requirements for plasma transport and storage hinder VL testing in resource-limited settings (RLS). Validating dried blood spots (DBS) for VL testing can improve access to VL monitoring. We evaluated the performance of DBS prepared in clinical settings using three simplified spotting modalities for VL monitoring in children.

Materials & Methods: Children (<15 years) on ART ≥6 months were enrolled at 12 clinics in Kenya. A routine plasma sample and one venous DBS (V-DBS) using a disposable transfer pipette were prepared using whole blood obtained by venipuncture; two additional DBS cards were prepared from finger-prick capillary blood using a microcapillary tube (M-DBS) and by directly spotting (D-DBS). Samples were tested on Abbott m2000 platform; DBS results were compared with plasma results to determine VF at two DBS thresholds (≥1,000 and ≥5,000 copies/mL) and a constant plasma threshold of ≥1,000 copies/mL.

Results: Paired plasma and DBS-VL results from 350 children were included; median age and time on ART were 6.6 years (IQR 3.8-9.0) and 40.9 months (IQR 24.3-60.0), respectively. At a ≥1,000 copies/ml threshold, sensitivities for detecting VF on V-DBS, M-DBS and D-DBS were 86.8% (95% confidence interval [CI] 79.4-92.2), 87.0% (95%CI 79.4-92.5), and 84.7% (95%CI 77.0-90.7), respectively, with corresponding specificities of 90.5% (95%CI 85.8-94.0), 93.2% (95%CI 89.0-96.1), and 92.9% (95%CI 88.7-95.9). Kappa values for V-DBS, M-DBS and D-DBS were 0.77 (0.69-0.84), 0.80 (CI 0.73-0.87), and 0.78 (CI 0.71-0.85), respectively, indicating excellent agreement with plasma at that cut-off. At a ≥5000 threshold, sensitivities for V-DBS, M-DBS and D-DBS were 81.8% (95%CI 73.8-88.2), 82.6% (95%CI 74.4-89.0), and 78.8% (95%CI 70.3-85.8), respectively, with corresponding specificities of 97.3% (95%CI 94.2-99.0), 97.7% (95%CI 94.8-99.3), and 98.2% (95%CI 95.5-99.5). Kappa values for V-DBS, M-DBS and D-DBS were 0.82 (0.75-0.88), 0.83 (CI 0.77-0.89), and 0.80 (CI 0.74-0.87). At ≥1000 cut-off, false negative misclassification rates were 13.2%, 13.0%, and 15.3% for V-DBS, M-DBS and D-DBS respectively, while false positive misclassification rates were 9.5%, 6.8%, and 7.1%. At the ≥5000 copies/ml cut-off, false negative misclassification rates increased to 18.2%, 17.4%, and 21.2% while false positive misclassification decreased to 2.7%, 2.3%, and 1.8% for V-DBS, M-DBS and D-DBS, respectively.

Conclusions: Even when not prepared in ideal laboratory settings, all three simplified DBS collection methods worked well for identifying VF in children using the Abbott m2000 platform. This study demonstrated that DBS-VL can be used in clinical sites in RLS to improve and expand access to VL monitoring. Because minimizing the false negative misclassification rate is preferred from a clinical and programmatic standpoint, DBS-VL at the 1,000 cut-off should be considered for identifying VF in children on ART.

No conflict of interest

Abstract: O_03

Time to First-Line ART Failure and Switch to Second-Line ART in the IeDEA Pediatric Cohort

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Background: There are limited data on durability of first-line antiretroviral treatment (ART) in children in resource-constrained settings. The objectives of this study were to determine the time from first-line ART initiation to treatment failure and to assess the time from failure to initiation of second-line ART in children.

Materials & Methods: This study was a collaboration between five regional Pediatric Cohorts within The
International Epidemiologic Databases to Evaluate AIDS (IeDEA) Consortium. Each IeDEA region harmonizes patient-level data collected during routine clinical care at affiliated HIV-care and treatment sites. Children initiating their first ART regimen between age 2 and 14 years were eligible. The outcomes of interest were: 1) ART failure defined by clinical (new or recurrent WHO 3/4 event or increase in WHO stage), immune (CD4 count <200 or CD4% <10% for children 2-5 years; CD4 count <100 cells/µl for children ≥5 years), and viral (VL ≥5,000 copies/µl) parameters at ≥24 weeks of ART; 2) Change to second-line ART defined as a class change in the backbone (e.g. change from an NNRTI to a PI) plus a change in ≥1 NRTI; 3) death and loss to follow-up (LTFU; ≥6 months without a clinic visit). Cumulative incidence was computed for first-line failure and second-line initiation respectively, with death or LTFU treated as a competing event. A cause-specific proportional hazards model was used to identify factors associated with each outcome.

Results: Outcomes of 21,977 children from Asia-Pacific (8.6%), Central (0.2%), East (32.3%), Southern (52.8%) and West (6%) Africa were analyzed. The median age at ART initiation was 6.8 (IQR 4.4-9.7) years and 49.4% were female. Median CD4% for children ≤ 5 years was 15% (IQR 8.0-24.4) and CD4 count for children > 5 years was 240 cells/µl (IQR 91-429). Most children initiated NNRTI-based ART (98.3%); 1.4% initiated PI and 0.3% triple NRTI-based ART. Failure was identified in 6,091 children and 4,257 died or were LTFU. At 1 year after ART initiation 12.7% (95%CI: 12.3-13.2) were dead/LTFU and 14.9% (95%CI: 14.4-15.4) had failed; by 5 years, the rates were 25.4% (95%CI: 24.7-26.2) and 39.1% (95%CI: 38.3- 40.0), respectively. Factors associated with higher failure rates were male sex, older age at ART initiation and region while starting non-NNRTI based ART was associated with lower rates. Factors associated with increased rates of death/LTFU were younger age at ART initiation, starting triple-NRTI ART, and region while starting PI-based ART was associated with lower rates. At 1 year after failure, 1.8% (95%CI: 1.5-2.2) were dead/LTFU and 9.5% (95%CI: 8.7-10.3) had changed to second line; by 5 years the rates were 4.7% (95%CI: 3.9-5.7) and 35.6% (95%CI: 33.5- 37.8), respectively. Factors associated with higher rates of change to second line were male sex, older age, starting non-NNRTI based ART, and region.

Conclusions: High rates of death/LTFU and first-line failure were identified in children 5 years after ART initiation. Of children meeting criteria for failure, only a third were changed to second-line ART by 5 years. Despite low rates of change to second line, death/LTFU rates were low.

No conflict of interest

Abstract: O_04

Stavudine: a viable drug option for children in resource limited settings?

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Background: Abacavir (ABC)-containing antiretroviral treatment (ART) regimens as first-line treatment for children have replaced the routine use of stavudine (d4T) to avoid d4T-related toxicities such as fat redistribution syndrome and dyslipidaemias. However, d4T is still utilised as a freely available and inexpensive option in resource limited settings. Should virally-suppressed children tolerating d4T be switched to an ABC-containing regimen?

Methods: A randomised clinical trial (Neverest 3) investigating the virological efficacy of an efavirenz (EFV)-containing ART regimen as long-term maintenance therapy in 300 nevirapine-exposed children, was conducted at Rahima Moosa Mother and Child Hospital, Johannesburg, South Africa. As part of the main study, 8 weeks prior to the EFV randomisation, children between the ages of 3-5 years who were virally suppressed to <50 copies/mL on lamivudine (3TC)/d4T/ritonavir-boosted lopinavir (LPV/r), and who showed no evidence of clinically recognisable lipodystrophy, were randomised to switch to ABC or remain on d4T. Follow-up included regular monitoring of viral load, CD4 count, fasting lipids, anthropometric measurements, and the development of lipodystrophy.

Results: Of the 300 enrolled (average age 4.2 years) 237 (79%) had been initiated on 3TC/d4T/LPV/r, at a mean age of 9 months. 71% (N=213) of enrolled children were eligible for randomisation; 107 switched to ABC (47.7% male), and 106 remained on d4T (47.2% male). Randomisation groups did not differ significantly at baseline. Un-blinded clinician assessment of the presence of possible/definite lipodystrophy changes identified consistently more children in the d4T arm through 48 weeks, although only significant at 12 (10.4%, 2.9%, p=0.030), and 40 weeks (15.7%, 4.9%, p=0.011) post-randomisation. Mean total cholesterol (4.7 ± 0.8, 4.4 ± 0.9 mmol/l, p=0.02) and the proportion of children with elevated LDL (25.2% vs. 10.9%, p=0.02) was higher in children switched to ABC at 8 weeks after the switch. However, at 48 weeks post-EFV randomisation, the d4T vs. ABC groups did not show significant differences in mean total cholesterol (4.4 ± 0.8, 4.4 ± 0.9 mmol/l); proportion of children with elevated LDL (10.8% vs. 11.8%); or mean triglycerides (1.1 ± 0.5, 1.1 ± 0.6 mmol/l). In addition, mean weight-for-age-z-score (-0.72 ± 1.0, -0.72 ± 1.0); mean CD4% (36.4 ± 6.9, 36.5 ± 6.7); or number of children with a non-suppressive viral load >50 copies/mL (6 (5.9%), 10 (9.7%)) did not differ significantly.

Conclusion: While we observed transient elevations in lipids among young virally-suppressed children who switched to ABC, these alterations did not persist through a year of follow up, and the prevalence of lipodystrophy was consistently lower among this group. Our findings suggest that even among virally-suppressed children tolerating d4T, there may be a benefit of switching to an ABC-containing regimen.

No conflict of interest

Abstract: O_05

Safety and efficacy of a rilpivirine-based regimen in HIV-infected treatment-naïve adolescents: Week 24 primary analysis of the PAINT phase II trial

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Background: Rilpivirine (TMC278) is a non-nucleoside reverse transcriptase inhibitor approved in combination with other antiretrovirals to treat HIV-1-infected, antiretroviral treatment (ART)-naïve adults with viral load (VL) ≤100,000 copies/mL. PAINT (NCT00799864) is an ongoing, Phase II, open-label, 48-week, 2-part trial in HIV-1-infected ART-naïve adolescents (12 to ≤18 years old). Based on pharmacokinetic, tolerability and efficacy data up to week 4 (Part 1), rilpivirine 25mg qd was the dose selected. Here we report the safety and efficacy in the 24-week primary analysis of Part 2.

Methods: Patients were recruited from sites in India, Thailand, Uganda, South Africa and the USA. Part 1b and 2 recruited only patients with screening VL ≤100,000 copies/ml. All patients received rilpivirine 25mg qd, taken with a meal in combination with two investigator-selected nucleoside/nucleotide reverse transcriptase inhibitors (N[t]RTIs). The primary efficacy endpoint was the proportion of patients with VL <50 copies/mL at Week 24 (virologic response, time-to-loss-of-virologic-response algorithm).

Results: Of 36 treated patients, 56% were female and 89% Black or African American, mainly from South Africa (56%) and Uganda (31%), and 67% received emtricitabine/tenofovir, 22% lamivudine/tenofovir and 11% lamivudine/zidovudine. Overall, 75% (27/36) of patients achieved virologic response at Week 24, 86% (24/28) in patients with baseline VL ≤100,000 copies/ml and 38% (3/8) in patients with VL >100,000 copies/ml. Nine patients (25%) discontinued by Week 24 for virologic failure (n=7), adverse event (AE, pulmonary tuberculosis [n=1]) and other reasons (n=1). The median increase in $CD4^+$ cell count from baseline at Week 24 (non-completer=failure) was 165 cells/mm^3. Thirteen patients (36%) reported an AE considered possibly related to rilpivirine, most commonly (not including investigations) somnolence (14%), rash (6%) and nausea (6%). One patient (3%) experienced a serious AE possibly related to rilpivirine (drug hypersensitivity; hospitalization for rash). Most AEs were grade 1 or 2. Grade 3 or 4 AEs (regardless of causality) were malaria (n=2), blood phosphorus decreased (n=1), pancreatitis (n=1), and depression, suicidal ideation and suicide attempt (in the same patient).

Conclusions: Rilpivirine 25mg qd in combination with 2 N[t]RTIs was effective and generally well tolerated over 24 weeks for the treatment of HIV-1-infected, ART-naïve adolescents with VL ≤100,000 copies/ml.

No conflict of interest

Abstract: O_06

Safety, Efficacy and Pharmacokinetics of the Integrase Inhibitor-Based Stribild Single-Tablet Regimen in HIV-infected Treatment-Naïve Adolescents Through 24 Weeks

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Background: The Stribild single-tablet regimen contains elvitegravir (EVG) 150 mg, the pharmacoenhancer cobicistat (COBI) 150 mg, emtricitabine (FTC) 200 mg and tenofovir disoproxil fumarate (TDF) 300 mg. The safety, efficacy, and pharmacokinetics of Stribild were evaluated through 24 weeks in adolescents in the initial Part A of a prospective, 48-week, single-arm, open-label trial.

Methods: Treatment-naive patients 12 to < 18 years of age with HIV-1 RNA > 1000 copies/mL (c/mL), CD4 counts > 200 cells/uL and eGFR (Schwartz) >90 mL/min received Stribild once daily. Adverse events (AE), routine laboratory tests and HIV-1 RNA (Roche TaqMan 2.0) were assessed through Week 24. Stribild plasma pharmacokinetics were assessed at steady state.

Results: Fourteen patients were enrolled, with a median age of 16 years (range: 13 to 17), 64% male, 29% Asian, 64% black and 7% white. At baseline, median CD4 count was 442 cells/uL and mean serum creatinine (sCr) was 0.77 mg/dL. Eight AEs assessed as related to Stribild occurred in 3/14 subjects (21.4%); these AEs were mild, predominantly (6/8) gastrointestinal, and did not require discontinuation. The mean increase in sCr was +0.08 mg/dL from baseline at Week 4 and +0.07 mg/dL from baseline at Week 24. There were no deaths, related SAEs, related nephrotoxicities, or related grade 3+ laboratory abnormalities. At the Week 24 efficacy endpoint, HIV-1 RNA was < 50 c/mL in 11/14 subjects (79%) and < 400 c/mL in 13/14 subjects (93%). The 14th subject discontinued Stribild due to pregnancy at Week 12, at which point her HIV-1 RNA was < 50 c/mL. Median CD4 count increased to 708 cells/uL at Week 24. No subject met criteria for virologic failure or resistance testing. The component antiretroviral steady state exposures (EVG, COBI, FTC and TFV) were comparable to adults.

Conclusions: Stribild was well-tolerated and effective in treatment-naive adolescents through 24 weeks and provided steady state exposures comparable to adults. Slight, stable increases in sCr were consistent with those seen with a cobicistat-containing regimen in adults and were not associated with nephrotoxicity. All subjects taking Stribild at Week 24 exhibited antiviral responses of < 400 c/mL.

Conflict of interest: Authors Liu, Custodio, Bennett, Cheng, and Quirk are employees of Gilead Sciences, Inc.

Abstract: O_07

Rationalization of the Pediatric Antiretroviral Formulary to Optimize Pediatric Antiretroviral Treatment in Malawi

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Introduction: The pediatric ARV market is challenged by low demand spread across multiple, redundant formulations creating instability and delays to country level supplies of drugs. A strategy to overcome this dynamic is for country programs to limit procurement to a rationalized list of pediatric ARVs. Rationalization increases volumes around optimal products, simultaneously increasing supply stability and generating efficiencies which decrease ARV costs.
In 2011, a series of workshops held in Malawi focused on decreasing the number of pediatric ARV formulations procured to a limited set of optimal products, such as fixed- dose combination (FDC) tablets instead of syrups and single drug formulations.

Methods : To assess the impact of Malawi's pediatric ARV formulary rationalization, the unit costs and product lead times for all products used to make up the recommended regimen, AZT + 3TC + NVP were compared for the years 2010-2013. Data was extracted from the UNITAID-CHAI Pediatric Program ARV tracker which documented all transactions related to pediatric ARV procurement in Malawi during this time period.
Direct comparison was made between:
1. Number of distinct pediatric ARV formulations procured (syrup vs. single tablets vs. triple FDC)
2. Product cost per patient per year (PPPY) for a 10 – 14 kg child
3. Shipping-related costs (PPPY) including freight cost; and procurement, handling and insurance fees.
4. Average lead times, defined as the number of days elapsed between the procurement order date and the invoice date

Results: After rationalization Malawi reduced the total number of pediatric ARV formulations procured from 23 to 8. A total unit cost savings of over 70% was achieved between 2010 and 2013 for products needed to make up the regimen now used by more than 90% of pediatric ART patients in Malawi . This was primarily driven by the lower product cost of FDC's compared to syrups though additional efficiencies contributed, such as shipping-related expenses which decreased over 95% PPPY during this time period.
Average lead times declined from nearly 3 months for all syrups, singles, and FDCs procured in 2010 to approximately one month for FDCs in 2013; an 85% reduction in average lead time. Variation in lead times for individual drugs was also eliminated by procurement of FDC's so that simultaneous availability of all drugs needed for a complete regimen could be assured while reducing the resources and effort needed for stock management and storage of multiple units.

Conclusion: After rationalization of the national pediatric ARV formulary Malawi streamlined the supply chain to significantly decrease the unit cost of pediatric ARVs and improve lead times for products. A model optimal pediatric ARV formulary has been developed by the Intragency Task Team for the Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and Children (IATT). Country adaptation of the IATT list and rationalized procurement is now recommended as a mechanism to ensure that high quality drugs for children living with HIV continue to be available at the right time and at affordable prices.

No conflict of interest

Abstract: O_08

A View on Pregnancy among HIV Perinatally Infected Adolescents

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Background: Since 1985 our hospital has followed 1,200 cases of HIV-perinatally infected (HPI) children. The increasing availability of antiretroviral drugs in the mid 1990's has resulted in a substantial rise in life expectancy and quality of life to these children, so that escalating number of them is surviving to adolescence and beyond. During 2010 we noticed the first cases of pregnancy among HPI adolescents. This study was aimed to explore the details of this phenomenon.

Materials and Methods: From 127 HPI girls 14 to 21 years old, 30 became pregnant during adolescence at least once. These 30 adolescents were submitted to a guided interview. Clinical and laboratorial data were obtained from medical records. The study was approved by our Institutional Review Board.

Results: Pregnancies were reported in 23.6% of the 127 adolescents, making a total of 39 pregnancies. The group presented four spontaneous miscarriages. No provoked abortion was reported. Only 24 adolescents (92.3%) declared total adherence to prenatal and use of antiretroviral drugs. Lopinavir/ritonavir was part of the prescribed antiretroviral regimen in 82.6% of the pregnancies.CD4 cells count during the first weeks of pregnancy was available in 26 cases and varied from 22 to 1443 cells/mm³. In 9 cases CD4 cells count were <350 cells/mm³. CD4 cells count was obtained in 27 cases at delivery and ranged from 10 to 1431 cells/mm³. In 10 cases CD4 cells count were <350 cells/mm³.Viral load during the first weeks of pregnancy was obtained in 26 cases. Nine (34.6%) showed undetectable values and the remaining showed values ranged between 151 and 638.360 copies/mm³.By the time of delivery 46% showed undetectable viral loads and the remaining presented values from 260 to 67.121 copies/mm³. Just 50% of them showed viral load values under 1,000 copies/mm³.Mode of delivery was obtained in 29 cases and 90% were elective cesarean section while vaginal delivery was reported in 3 cases (10%). From 35 newborns, 11 were considered as premature (less than 38 weeks of pregnancy) and 5 children showed low weight at birth. All children showed good clinical conditions at birth. All newborns received Zidovudine prophylaxis and 89.6% received PCP prophylaxis. Just one child (2.3%) showed to be HIV-infected.The pregnancy was desired in 51.4% of the cases. All adolescents are taking care of their children and reported that maternity brought 'a new reason for living'.From the sexual partners 86.7% were in a fixed relationship at conception, 96.7% were HIV seronegative and 80% were aware of the HIV status of the adolescents. Two couples submitted to a domestic artificial insemination.

Conclusions: Despite awareness of and knowledge about reproductive health, HIV transmission and contraceptive methods, the incidence of pregnancies in this group is the same observed among uninfected adolescents in our country.The reported adherence to prenatal care and antiretroviral use was discrepant to the viral loads observed. This fact raised a doubt on the reported level of compliance to the antiretroviral drugs. Despite this scenario, mother-to-child transmission rate in this setting was 2.3%.

No conflict of interest

Abstract: O-09

Tenofovir DF (TDF) Plus an Optimized Background Regimen (OBR) in HIV-1 Infected Adolescents Failing a Regimen: Study GS-US-104-0321 Final Results

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Introduction: TDF is a preferred nucleoside reverse transcriptase inhibitor for treatment of HIV-1 infection. We describe the final results of Study 321 in antiretroviral (ARV) treatment-experienced adolescents with HIV-1 infection.

Materials and Methods: HIV-1 infected patients 12 to <18 years of age failing an ARV regimen with HIV-1 RNA ≥ 1000 copies/mL (c/mL) were randomized to TDF 300 mg or placebo (PBO) once daily plus an OBR for 24-48 weeks. Three subgroups received open label (OL) TDF in study extensions: subjects with baseline HIV-1 RNA ≥1000 copies/mL (c/mL) initially randomized to TDF (TDF/TDF subgroup), subjects who failed randomized PBO plus OBR with HIV-1 RNA ≥1000 c/mL and switched PBO to TDF (PBO/TDF ≥1000 subgroup), and PBO recipients with HIV-1 RNA <1000 c/mL who switched PBO to TDF (PBO/TDF <1000 subgroup). Safety (adverse events [AE] and laboratories) and efficacy (HIV-1 RNA [Roche Amplicor]) were assessed every 12 weeks until all subjects discontinued or reached age 18. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry (DXA) every 48 weeks. BMD Z-scores were adjusted for height-age—age where 50th percentile corresponds to the subject height—for subject heights less than median height for 20 years-olds (US CDC growth chart). Proportion with HIV-1 RNA < 50 copies/mL (missing=failure) was assessed by subgroup.

Results: 81 subjects received TDF in the OL extensions (43.2% male, 53.1% white, 29.6% black, median age 14 years, mean CD4 422 cells/mm^3). At TDF baseline, 61 had HIV-1 RNA ≥1000 c/mL (44 in TDF/TDF, 17 in PBO/TDF ≥1000) and 18 had HIV-1 RNA <1000 c/mL (PBO/TDF<1000). Mean TDF treatment duration was 104.5 weeks (maximum 294 weeks). No subject died. Eight of 81 subjects (9.9%) discontinued the OL extensions for safety, tolerability or efficacy reasons, none due to AE. 38.3% maintained a TDF adherence rate of ≥95%. At Week 144, proportion with HIV-1 RNA <50 c/mL were 7/23 (30.4%), 0/2 and 5/12 (41.7%) and CD4 change from baseline was +188 cells/mm^3, +33 cells/mm^3 and -88 cells/mm^3 in the TDF/TDF, PBO/TDF≥1000, and PBO/TDF<1000 subgroups, respectively. One of 57 subjects with resistance testing developed K65R. The most frequent AEs were sinusitis (32.1%), cough (29.6%) and vomiting (25.9%). Median change in serum creatinine at Week 144 was +0.16 mg/dL (n = 25). Increases from baseline in median spine (+12.70%, n=26) and total body (TB) BMD (+4.32%, n=26) and height-age adjusted Z-scores (n=21; +0.457 for spine, +0.152 for TB) were observed at Week 144. Thirteen of 81 subjects (13.6%) had >4% decreases in BMD from baseline, 3 of whom had low BMD (Z-score <-2.0 at any time point).

Conclusions: Despite suboptimal adherence, some adolescent subjects achieved and maintained virologic and immunologic responses to TDF plus OBR. Viral resistance to TDF developed infrequently. TDF was well tolerated in HIV-1 infected adolescents. No subject died or discontinued OL TDF for tolerability. Creatinine increases were consistent with normal GFR changes in a population approaching adulthood, and BMD increased from baseline. TDF once daily can be considered as part of an ARV regimen in difficult-to-treat, HIV-infected adolescents.

Conflict of interest: I am an employee and stockholder of Gilead Sciences, the sponsor of the study summarized in the abstract.

Abstract: O_10

Prevalence of and Progression to Abnormal Non-Invasive Markers of Liver Disease (APRI and FIB-4) among US HIV-infected Youth

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Background: HIV infection, even in the absence of viral hepatitis co-infection, may contribute to liver disease. Non-invasive surrogate markers of liver disease [FIB-4 and APRI (aspartate aminotransferase-to-platelet ratio index)] have been investigated and validated in HIV/HCV co-infected adults, but have been studied less in children.

Methods: FIB-4 [age*AST/platelet#*$ALT^{1/2}$] and APRI [100*(AST/AST ULN)/platelet#] measures were evaluated in two prospective cohorts (REACH and PACTG 219/219c) of HIV-mono-infected and HIV-uninfected youth. We compared FIB-4 and APRI measures at ages 15-20 years between HIV-infected and HIV-uninfected youth based on a single visit, and also longitudinally modeled trends in these measures in HIV-infected youth with ≥2 visits to compare those with behavioral vs perinatal HIV infection using mixed effect linear regression adjusting for age, gender and race/ethnicity.

Results: Among 1780 participants, 1302 (73%) had measures from ≥2 visits (median follow-up=2 years). 41% were male, 57% black non-Hispanic and 27% Hispanic. More HIV-infected than uninfected youth had an APRI score >0.5 (12% vs 3%) suggesting at least subclinical fibrosis, and slightly more had APRI >1.5 (2% vs 1%), suggesting significant fibrosis (p=0.002). After adjustment, the mean APRI and FIB-4 were 38% (p<0.001) and 15% (p<0.001) higher, respectively, in HIV-infected compared to uninfected youth. APRI and FIB-4 were higher in males than females by 34% and 20%, respectively (p<0.001). The mean APRI and FIB-4 did not differ between those with behavioral and perinatal HIV infection.
Over time, FIB-4 scores increased significantly among all HIV-infected youth (6% per year) whereas APRI scores increased only among those with perinatal HIV infection (2% per year). The incidence per 100 person-years of follow-up (95% CI) of progression for APRI at thresholds of >0.5 (mild/moderate fibrosis) and >1.5 (advanced fibrosis) were 7.4 (6.3-8.5) and 1.4 (1.0-1.9), respectively. The incidence rate of progression for FIB-4 at thresholds of >1.5 (mild/moderate fibrosis), >2.5 (mild/moderate fibrosis) and >3.25 (advanced fibrosis) were 1.6 (1.2-2.2), 0.6 (0.4-1.0) and 0.3 (0.2-0.6), respectively.

Conclusions: The mean APRI and FIB-4 scores were higher among HIV-infected youth and remained so after adjustments. Progression to scores suggesting subclinical fibrosis or worse was common. More research is needed on the clinical utility of non-invasive methods to assess liver disease among HIV-infected adolescents.

No conflict of interest

Abstract: O_11

3TC/FTC Monotherapy vs. Continuing Failing cART as a Bridging ART Strategy in Persistently Non-adherent HIV-infected Youth with M184V Resistance: Results of IMPAACT P1094

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Introduction: There is no clear consensus for management of HIV-infected youth whose persistent non-adherence leads to virologic failure (VF), which may lead to resistance, immunologic failure (IF), and limited treatment options. In the presence of the M184V resistance mutation, 3TC (or FTC) monotherapy (Mono) does not suppress viral replication or select for additional drug resistance mutations, but it reduces viral fitness, has limited side effects, and has adherence advantages over standard multi-pill combination antiretroviral treatment (cART) regimens due to simplicity. The strategy is employed in settings where persistent nonadherence limits treatment options. P1094 was designed to compare the immunologic outcome of continuing failing cART vs. switching to Mono as a 'bridging strategy' to subsequent suppressive cART for non-adherent patients with pre-existing M184V resistance while providing adherence interventions pending readiness for a new cART regimen.

Materials & Methods: Participants with documented non-adherence (e.g., self or pharmacy report, persistent VF with no documented resistance), M184V resistance mutation at or prior to screening, CD4≥100 cells/mm^3 (with DSMB mandated close monitoring) and VF (defined as HIV-1 plasma RNA ≥400 copies/mL) were enrolled between May 2011 and December 2012 and randomized to continue failing cART vs. switch to Mono. The primary endpoint was time to first ≥30% CD4 decline from baseline or development of CDC class C events. Kaplan-Meier (K-M) curves were used to assess the 28-week outcome in an intent-to-treat analysis.

Results: The study was discontinued in February 2013 due to slow accrual at United States sites and long regulatory processing times delaying opening at international sites. We present the results for all 33 perinatally HIV-infected participants enrolled until study closure (16 randomized to continuing ART and 17 to Mono). Participants were median age 15 years (IQR 14-20), 68% female, and 52% black. Median entry CD4 and viral load were 472 cells/mm^3 (IQR 384-651) and 4.0 $\log_{10}$HIV-1 RNA copies/ml (IQR 3.2-4.5), respectively. A median of 4 interventions (e.g., counseling, text reminders, directly observed therapy) had been used to address non-adherence prior to study. Five participants, all in the Mono arm, reached the primary endpoint for CD4 decline (log-rank test p=0.03). The K-M estimate of probability of failure at 28 weeks was 0.41 (standard error 0.14). There were no CDC class C events or deaths and no difference in adverse events between the arms.

Conclusions: Non-adherent participants randomized to Mono were more likely than those maintained on failing cART to sustain ≥30% CD4 decline, suggesting that even as a bridging strategy to suppressive cART, better alternatives to Mono such as higher barrier to resistance cART and novel adherence and treatment strategies should be developed and used for youth failing cART because of persistent non-adherence.

No conflict of interest

Abstract: O_12

Safety of Triple Drug Antiretroviral Prophylaxis in High Risk HIV-Exposed Neonates

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Introduction: Triple drug combination antiretroviral therapy (cART) at treatment doses has routinely been prescribed in our institutions to infants born to mothers with inadequate HIV virologic suppression (documented or suspected) late in gestation. The purpose of this study was to evaluate the safety of neonatal cART in this setting.

Materials & Methods: HIV-exposed children born prior to January 2014 were eligible if they were initiated on cART within 72 hours of birth. Data were extracted by retrospective chart review. Laboratory measures of possible toxicity were compared to a cohort of zidovudine monotherapy (ZDV) recipients from one institution.

Results: 136 cART- and 145 ZDV-treated infants were included. Neonatal cART consisted of ZDV/3TC/nevirapine in 41% (n=56), ZDV/3TC/nelfinavir in 54% (n=73) and ZDV/3TC/lopinavir/r in 5% (n=7). In 79% of cART recipients maternal viral load was known to be elevated at or just prior to delivery (median 756 copies/mL; IQR 154, 6326). Other reasons for cART included poor adherence (40%), late diagnosis (20%), no antenatal care (8%) and treatment refusal (8%). Symptoms or signs potentially related to cART included rash (11%), irritability (8%), jitteriness (6%), vomiting (5%), lethargy (4%) and diarrhea (4%). There was a significant difference in median hemoglobin at one month of age in cART recipients vs. ZDV recipients (102 g/L vs. 108 g/L, p=0.05); at 2 and 6 months of age no significant difference in hemoglobin was noted (104 g/L vs. 105 g/L, p=0.40 and 119.5 g/L vs. 122 g/L, p=0.10 respectively). At 1 month of age, there were no significant differences in median neutrophil count (1520/mm^3 vs. 1540/mm^3 p=0.90), ALT (17 U/L vs. 19 U/L, p=0.30) or lactate (3.20 mmol/L vs. 2.7 mmol/L, p=0.10) between the two groups. Subgroup analysis of nevirapine-based versus protease inhibitor-based cART showed that the former group had lower serum lactate at 1 month of age (2.90 mmol/L vs. 3.70 mmol/L, p<0.001); there were no differences in hemoglobin (103.5 g/L vs. 101 g/L, p=0.60) and neutrophil count (1460/mm^3 vs. 1600/mm^3, p=0.40). Premature treatment discontinuation due to possible adverse events occurred in 7% of cART recipients (n=3 nevirapine based, n=7 protease inhibitor based) vs. 3% (n=4) of ZDV recipients (p=0.07). There was no significant difference in discontinuation rate between nevirapine-based cART and PI-based cART (5% vs. 9%, p=0.4). Reasons for premature discontinuation of cART included rash (n=2) hemoglobin <80 g/L (n=2), neutropenia <500/mm^3 (n=1), persistent vomiting (n=1), possible pancreatitis (lipase 162 U/L; n=1), elevated CPK (1243 U/L; n=1) and elevated GGT (494 U/L; n=1).

Conclusions: Adverse events were more common in cART recipients, but in most cases these were mild and self resolving. The lack of difference in one month hemoglobin between nevirapine-based and PI-based cART suggest that the more severe anemia observed in cART recipients is likely attributable to dual nucleoside analogue therapy. Controlled trials are needed to further evaluate the safety, efficacy, pharmacokinetics and benefits of cART as prophylaxis in neonates at high risk of perinatal infection.

No conflict of interest

Abstract: O_13

Nevirapine Pharmacokinetics in HIV-exposed Neonates Receiving Triple Combination Antiretroviral Therapy as Post-Exposure Prophylaxis

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Background: Neonates at increased risk of HIV infection receive nevirapine (NVP)-based triple combination antiretroviral therapy (cART) as HIV-post exposure prophylaxis (HIV-PEP) at our centers. The nevirapine dose used is higher than has been previously studied in HIV-exposed neonates and aims to achieve therapeutic rather than prophylactic drug levels. Our aim was to evaluate the pharmacokinetics and safety of this dosing regimen using therapeutic drug monitoring (TDM).

Methods: Neonates given NVP-based cART-HIV-PEP between April 2012 and January 2014 were included. Empiric NVP dosing was 150 mg/m^2 orally once daily for 14 days, then 150 mg/m^2 every 12 hours for 14 days (total 4 weeks). NVP levels were measured pre-dose (trough) at weeks 1 and 2, and pre-dose (trough) and 1 and 4 hours post-dose at week 4. Informed consent was obtained for the 4 week pharmacokinetic evaluation. Doses were adjusted at the 1 and 2 week visits if nevirapine trough levels (NVP-T) fell outside the therapeutic range of 3-8 mg/L. NVP plasma levels were measured using validated liquid chromatography coupled to tandem mass spectrometry. Pharmacokinetic parameters were calculated using non-compartmental analysis with Phoenix WinNonLin 6.1 software.

Results: At least one NVP-T was obtained for 22 neonates and both trough and post-dose levels were obtained for 12/22 neonates for the 4 week pharmacokinetic evaluation. Neonates had a median gestational age (GA) of 37.2 weeks (30-41.7) and a median birth weight (BW) of 2.91 kg (1.05-3.61). Median (range) NVP-T's were 9.2 mg/L (1.6–25.4) at week 1, 4.1 mg/L (1.6–26.1) at week 2, and 3.8 mg/L (0.2- 17.1) at week 4. The proportion of therapeutic NVP-T increased from 43.8% (7/16) at week 1, to 66.7% (12/18) at week 2 and 83.3% (15/18) at week 4. Supra-therapeutic NVP-T's were observed in 50.0% (8/16) and 5.5% (1/18) at week 1 and 2, respectively. Median oral clearance (ClssF) was 2.97 L/kg/h (0.39-16.28) and median drug exposure (AUC_T) was 11.1 mg/L*hr (1.9-73.5). Increased drug exposure was correlated with lower GA (r = 0.437, p=0.05) and lower BW (r = 0.422, p=0.057). The most common laboratory abnormalities were asymptomatic hyperlactatemia (lactate>2.4 mmol/L)(n=14, 23.7%), neutropenia (ANC<1.5 x 10^9/L)(n=12, 20.4%), and anemia (Hb<115 g/L)(n=11, 18.6%). The majority of adverse effects were mild or moderate in severity (67.8% Grade 1, 23.7% Grade 2, 5.1% Grade 3, 1.6% Grade 4).No cases of vertical transmission, rash, or transaminitis occurred; premature treatment discontinuation was not required.

Conclusions: The current nevirapine dose achieved therapeutic levels for most patients as drug clearance increased with maturity. Lower empiric dosing given less frequently and/or close monitoring with TDM and dose adjustment as needed, may be required for low birth weight or premature infants. Nevirapine was well-tolerated and laboratory abnormalities were attributable to other causes.

No conflict of interest

Abstract: O_15

Creating Demand for and Retention in Maternal and Child Health(MNCH) including PMTCT services: A Randomized Community Based Peer Facilitator Intervention in Rural Zimbabwe

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Introduction: The adoption of WHO 2010 Option A PMTCT guidelines in Zimbabwe necessitated research to identify new strategies to increase demand for early first ANC attendance and increase retention of mothers in MNCH/ HIV care. This study tested whether peer-facilitated community support groups for pregnant women increased the number of pregnant women booking earlier for ANC and strengthened retention in MNCH/PMTCT services.

Materials & Methods: A pair-matched community randomized control trial of 8 pairs in one rural district in Zimbabwe was conducted, where the intervention health facility together with the community it serves received community based peer support group intervention for one year. Trained peer facilitators recruited pregnant women to form ANC support groups where peer facilitators shared information with their peers using modules, developed for this project, on general maternal and child health and PMTCT specific topics using participatory learning and problem-solving approaches. Baseline, end-term aggregate and longitudinal individual-level data were collected at all health facilities in the intervention and control communities. Matched pair data analysis was conducted using STATA version 12.1. Heterogeneity and homogeneity between the pairs was assessed and either fixed or random effect modelling was done to assess the overall effect of the intervention on demand and retention study indicators.

Results: A total of 1206 peers (women) were recruited into 143 ANC support groups by 24 trained peer facilitators during the 12 month intervention. The peers met bi-monthly in community support groups and had Peer Facilitator led discussion using project modules targeted at bringing awareness about the importance of early ANC attendance, retention, pregnancy and HIV. The intervention demonstrated significant improvements in the following: gestational age at booking was reduced by 1.7 weeks ($p < 0.001$); percentage of women booking at < 21weeks increased by 11% ($p=0.006$); percentage of women who had WHO recommended 4 or more ANC visits increased by 15% ($p < 0.001$) Percentage of institutional deliveries increased by 10.5%, though this was not statistically significant.

Conclusions: The community-based peer support group was effective in improving time at which women present for their initial ANC visit, completing the WHO-recommended four ANC visits, and facility deliveries. This study adds to the body of knowledge the effect of community based peer facilitator intervention on demand for early ANC attendance.This intervention has the potential to increase demand and improve retention in MNCH services if scaled up, more so now as Zimbabwe transitions to the implementation lifelong antiretroviral treatment for pregnant and lactating women.

No conflict of interest

Abstract: O_16

Oral abstract presentations

Measuring the impacts of health facility reinforcement and EID and EPI service integration on testing and immunization services in Southern Province, Zambia

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Background: Early identification of HIV positive infants is critical to reducing HIV-related infant mortality in Zambia. However, it is estimated that only thirty percent of HIV-exposed infants are tested for HIV each year, and adherence to national guidelines to test mothers with unknown HIV status or re-test mothers who previously tested HIV-negative is even lower. We report findings of an evaluation that examined whether guaranteed supply of HIV testing materials or the integration of early infant diagnosis within routine immunization clinics would improve maternal and infant HIV testing rates without interfering with immunization services.

Method: The evaluation followed a cluster randomized design with 60 study health facilities randomized to one of three study arms (n=20 per arm):

- Simple Intervention Arm: Facilities received a guaranteed supply of antibody and dried blood spot (DBS) DNA PCR testing materials and a review and re- emphasis of existing testing guidelines from district health staff.
- Comprehensive Intervention Arm: Facilities received the Simple Intervention plus two additional components:
  1. Two training sessions on better integrating HIV-service delivery into under-5 clinics
  2. Introduction during the 6 week postnatal visit of opt-out HIV testing for all previously HIV-negative or unknown status mothers. This is in order to identify HIV-positive mothers for their own health and for prevention of mother-to-child transmission, and to identify previously unrecognized HIV-exposed infants and test them for HIV.
- Control arm: Facilities continued standard protocols.

This study included approximately 10,000 mother-infant pairs.
We collected information on the following variables: numbers of infants receiving DPT1, DBS tests administered, rapid tests administered, the proportion of positive rapid tests and the frequency of stock-outs of rapid tests and DBS kits. In addition, we conducted linear regression analysis to determine the effect of the comprehensive intervention on immunization uptake, which controlled for baseline immunization rates, antenatal care attendance rates, distance from the district health office, and time trends.

Results: Mid-evaluation results after three months of data collection indicate:

- No negative effect on the number of immunizations. Findings from the linear regression suggest a negligible change in DPT1 immunizations [0.6% increase, 95% CI: -12.1%, 13.4%] in comprehensive intervention facilities compared to control facilities.
- Stockouts of HIV test kits are a major constraint for health facilities. Across 40 intervention facilities, the research team had to re-supply facilities in danger of stock-out 34 times for Determine test kits, 20 times for UNIGOLD test kits, and 46 times for DBS.

Results on the impact of infant and maternal testing will be reported at the conference.

Conclusions: The results from the mid-study analysis of the data demonstrate that it is feasible to introduce opt-out maternal HIV testing and infant HIV testing at the 6 week postnatal visit at under-5 clinics without damaging immunization rates. To best utilize this integration of services at under-5 clinics, attention must also be paid to improving the supply chain for HIV testing commodities.

No conflict of interest

Abstract: O_17

Tuberculosis in HIV-infected children in Thailand: prevalence, incidence and mortality

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Background: Tuberculosis (TB) and HIV co-infection in children is a major global health concern. This study aims to estimate the prevalence and incidence of active TB in HIV-infected children, identify risk factors for TB infection and estimate survival rates among TB-HIV co-infected children in a large HIV cohort study in Thailand.

Materials & Methods: This retrospective study includes all HIV-infected children of less than 15 years old enrolled in the PHPT cohort in Thailand between 1999 and 2012. Screening of active TB was performed before initiating ART and at least every 6 months thereafter, based on interview, clinical examination and diagnosis on sputum and chest X-ray, and other examinations as necessary. HIV RNA levels and CD4 counts were routinely monitored and a complete blood count was performed at least every 6 months. Weight status was assessed using BMI *z*-scores from the WHO BMI-for-age standards. Prevalence was defined as the proportion of TB cases among all HIV-infected children, and incidence as the number of new TB cases divided by the total number of person-years of follow-up (PYFU). We assessed potential risk factors for TB infection (sex, age, BMI-for-age, HIV RNA, CD4 and complete blood count parameters) at ART initiation, using incidence rate ratios (IRR) from Poisson regression models. Survival rates were estimated using the Kaplan-Meier method and survival distributions were compared with a log-rank test.

Results: Of 839 HIV-infected children, 54% were female. At ART initiation, median age was 6.7 years (interquartile range (IQR): 2.4-9.6), HIV RNA load 5.0 $\log_{10}$ copies/mL (4.3-5.6) and CD4 10% (4-18). A total of 106 (12.6%) children were diagnosed with active TB, including 59 before and 47 after ART initiation. Among the 780 children not diagnosed with TB before ART initiation, the overall TB incidence rate was 8.9/1,000 PYFU (95% CI: 6.7-11.8) over a median follow-up of 7.7 years (IQR: 3.6-9.9). Median follow-up duration between ART initiation and TB diagnosis was 1.2 years (IQR: 0.2-4.8). TB incidence rates decreased steadily with ART duration, from 29.8/1,000 PFYU during the first year on ART to 5.0/1,000 PFYU after 5 years. Older children were at higher risk of TB infection (6-10 vs. 0-5 years: IRR=1.2; 11-15 vs. 0-5 years: IRR=2.2; p=0.046). After adjustment on sex and age, TB infection was associated with higher levels (above median) of HIV RNA load (IRR=2.9, p=0.009) and neutrophils (IRR=2.1, p=0.039), lower BMI (*z*-score<0: IRR=6.2, p=0.014) and lower levels (below median) of hemoglobin (IRR=3.6, p=0.001) and hematocrit (IRR=3.4, p=0.002) at ART initiation. Of the 47 children diagnosed with active TB after ART initiation, 13 died. Overall survival rates among TB-HIV co-infected children were 91%, 85% and 69% at 1, 5 and 10 years after initiating ART, as compared with 96%, 93% and 91% in HIV mono-infected children (p<0.001).

Conclusions: TB incidence was highest in the first year on ART. Higher mortality rates were observed among HIV-infected children with TB. Anemia, low BMI and high HIV RNA load at ART initiation are indicators that can help closely monitor children at risk of developing TB.

No conflict of interest

Abstract: O_18

The Impact of Isoniazid Preventive Therapy and Antiretroviral Therapy on TB Incidence in Children Living with HIV in Vietnam

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Introduction: Isoniazid preventive therapy (IPT) reduces the risk of tuberculosis (TB) disease for people living with HIV, but uptake of this intervention has been low. We describe the implementation of a pediatric IPT program in Vietnam, and the impact of IPT and antiretroviral therapy (ART) on incident TB disease.

Methods: An IPT program was initiated at Ho Chi Minh City Children's Hospital #1 (Peds1) in June 2011, based on the 2011 WHO TB/HIV Guidelines. We retrospectively reviewed health records of patients registered in HIV care at Peds1 during the period of July/2009 - June/2013 (2 years before and after IPT introduction). IPT initiation, completion, and side effects rates, and TB incidence rates by treatment group (IPT+/-ART) were evaluated.

Results: Of 582 patients screened for eligibility, 551 completed IPT (median age 7 years; 94% on ART). One patient was diagnosed with TB after positive screening. Eighteen discontinued IPT (due to side effects [6], parent choice [7], TB diagnosis [1], patient transfer [1], death [1] and loss to follow-up [2]), and 12 had not yet completed IPT. No TB cases were detected among patients who completed IPT (median 16 months post-completion); 2 patients with advanced HIV who stopped IPT for liver enzyme elevation died of suspected TB soon after discontinuation. During the 4-year period, 54 TB cases were diagnosed amongst 854 children during 26,652 patient-months of follow-up (PMFU). This included 51 cases pre-IPT and 3 after IPT initiation (post-IPT). This yielded TB incidence rates per 1000 PMFU: 10.49 in pre-IPT/pre-ART patients, 0 post-IPT/pre-ART, 2.34 pre-IPT/post-ART, and 0.27 post-IPT/post-ART. Using TB incidence rate in pre-ART/pre-IPT patients as the reference, incidence rate ratios for TB were 0.22 (95%CI 0.13-0.39) for pre-IPT/post-ART patients, and 0.025 (0.006-0.077) for post-IPT/post-ART (unable to calculate for pre-ART/post-IPT patients due to no TB cases in this group).

Conclusions: Our program had a 95% rate of completion of IPT, suggesting good tolerability among HIV-infected children. Patients who received ART had 78% reduction in TB incidence, while those who received both ART and IPT had 97% reduction. These results support the WHO recommendation for routine use of IPT in HIV-infected children.

No conflict of interest

Abstract: O_19

Effect of calcium and cholecalciferol supplement on bone mass accrual among perinatally HIV-infected adolescents with osteopenia

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Background: Low bone mineral density (BMD) is a common finding among HIV-infected adolescents. The study objective was to describe changes in BMD among perinatally HIV-infected adolescents with osteopenia before and after receiving calcium and cholecalciferol supplements.

Materials and methods: In 2011, we conducted a study to assess BMD among 101 Thai HIV-infected adolescents aged 12-20 years using dual-energy X-ray absorptiometry (DXA). Adolescents who had osteopenia, defined as lumbar spine (L2-L4) BMD < -2 z-score, received education about appropriate dietary intake and exercise. In 2013, we performed a second DXA assessment and tested serum 25-hydroxyvitamin D (25-OHD) levels. Adolescents who had persistent or newly developed BMD < -2 z-score were prescribed a 6-month course of a fixed-dose combination of elemental calcium 600 mg plus vitamin D3 200 IU twice daily. In addition, adolescents who had 25-OHD levels < 20 ng/ml received calcium 1000 mg/day and vitamin D2 60,000 IU weekly for 8 weeks prior to the 6-month supplement. After completion of the 6-month course of supplemental treatment, BMD and 25-OHD were measured again. The BMD z-score was calculated using age and sex-matched Thai adolescent norms. The signed-rank test was used to compare changes in BMD pre- and post-supplementation.

Results: At the second DXA, 24 adolescents (15 male, 9 female) had BMD < -2 z-score. Thirteen adolescents (54%) had persistently low BMD from their first assessments, and 11 (46%) were newly identified. The median (IQR) age was 16.0 (15.0-16.7) years and all except one were in Tanner stage 3-5. The antiretroviral regimens were PI- (67%) and NNRTI- based (33%). The median CD4 cell count was 693 cell/mm3 and 20 participants (83%) had HIV RNA < 40 copies/ml. The median 25-OHD level pre- and post-supplementation were 31.2 (23.6 -37.3) and 28.7 (24.2-35.8) ng/mL, respectively (p=0.57). The median (IQR) BMD pre- and post-supplementation were 0.76 (0.70-0.86) and 0.82 (0.78-0.92) g/cm2, respectively (p<0.001). The median (IQR) BMD z-score pre- and post-supplementation were -2.59(-3.02 to -2.35) and -1.90 (-2.51 to -1.60), respectively (p<0.001). Fourteen adolescents (58%) had BMD z-scores improved to better than -2 z-score after receiving supplement. Among 13 adolescents who had low BMD since their first assessment, the BMD gain over time without supplementation was 0.063 (0.047-0.096) g/cm2 after a median of 21 months, and 0.057 (0.040-0.066) g/cm2 after the 6-month supplementation period. The BMD z-score changes were -0.54 (-1.00 to 0.06) and 0.65 (0.13 to 1.20), respectively (p = 0.028).

Conclusions: Unlike reports from Western countries, our study shows an improvement of bone mass accrual among HIV-infected adolescents who had low BMD after receiving a 6-month course of calcium and cholecalciferol supplementation. This may be explained by the pre-selection of adolescents with baseline BMD < -2 z score during pubertal years, and nutritional issues including the inadequate intake of calcium and vitamin D among adolescents in our middle-income country setting. Additional research to confirm the benefit of supplementation on bone accrual is needed to help guide recommendations of whether and when supplementation could be beneficial in this population.

No conflict of interest

Abstract: O_20

The effect of antiretroviral therapy on tuberculosis incidence rate among adolescents and younger children living with HIV in Ethiopia

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Background: Adolescents constitute a significant proportion of people living with HIV in settings with limited resources. However, there is limited data on the occurrence of tuberculosis and other co-infections in this age group. We report preliminary results from a cohort of HIV infected adolescents treated and followed at three hospitals in Ethiopia. Our aim was to measure the burden of tuberculosis among adolescents and children living with HIV before and after treating with antiretroviral therapy (ART).

Material &Methods: We conducted a retrospective cohort study in three hospitals in Ethiopia between April-May 2014 as part of an adolescent HIV cohort study being rolled out to seven more sites. The study population constituted adolescents (age 10-19 years) and children (0-9 years) enrolled in chronic HIV care between January through 2005-December 31 2013. Trained nurses assisted by site data clerks did retrospective chart review using pre-tested data abstraction tool. We entered and analyzed the data using SPSS version 20. In this analysis, we focused on measuring proportion of tuberculosis (TB) before, at, and after enrollment into pre-ART and ART care. We also calculated TB incidence rates (IR) and incidence rate ratios (IRR) per 100 person-years of observation (PYO) with 95% confidence intervals in the two age groups before and after ART initiation using OpenEpi program.

Results: 237 patients (69 children and 166 adolescents) contributed 379.97 PYO in the pre-ART period of follow up. Out of these, 180 were put on ART and they contributed 847.33 PYO after ART initiation. Their median age was 11 years (IQR, 6-15 years), 55.7% were girls, and 41% were in advanced WHO clinical stage at presentation. Past history of tuberculosis was reported in 14.8% of the patients (15.9% adolescents vs. 14.3% in children) at baseline. Further, 11.8% had history of tuberculosis at enrollment into chronic HIV care. Thirty-five patients developed new TB during pre-ART follow up and 8 patients developed TB after ART initiation. The overall IR of TB during pre-ART follow up was 9.2 per 100 PYO (95% CI, 6.4-12.8) The IR was higher in children (IR=12.9, 95% CI=6.8-22.0) than in adolescents (IR=7.9, 95% CI=4.9-11.9) but the difference was not statistically significant (IRR=0.61, 95%CI=0.31-1.25). The IR dropped to 0.94 per 100 PYO (95% CI, 0.41-1.86) after ART initiation, making the IRR (ART versus pre-ART period) 0.10 (95% CI, 0.04-0.22, p<0.0001). ART use was thus associated with 90% reduction TB incidence rate (95% CI, 77.91%-95.24%).

Conclusions: TB is a major problem among adolescents and children living with HIV in the study setting during the pre-ART phase of care. ART is effective in preventing TB in this age group. The beneficial effect of other interventions such as IPT should be examined in adolescents and children using larger sample size. This age group should be prioritized both in TB and HIV prevention programs.

No conflict of interest

Abstract: O_21

CHAPAS 3: A randomised trial comparing stavudine vs zidovudine vs abacavir as NRTI backbone in NNRTI-based first-line ART in 478 HIV-infected children in Uganda and Zambia

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Background: Lipodystrophy is well-documented in adults/adolescents on stavudine (d4T), but there are few data in younger children receiving lower WHO-recommended doses.
Alternative NRTIs include abacavir (ABC), but its efficacy has been questioned in cohort studies, and zidovudine (ZDV) which may cause anaemia, particularly in malnourished children in endemic malaria areas. CHAPAS-3 was a randomised trial comparing 96-week toxicity and efficacy of d4T, ZDV and ABC in solid, scored, dispersible fixed-dose-combination (FDC) formulations given with lamivudine (3TC) and efavirenz (EFV) or nevirapine (NVP) in 478 Zambian/Ugandan children aged 1 month to13 years.

Methods: Between November 2010 and December 2011, 365 ART-naïve children were randomised to d4T (123), ZDV (112) or ABC (130) within double/triple FDCs; a further 113 ART-experienced children on d4T-containing ART for median 3.5(2.6,4.2) years, with viral load (VL) <50c/ml, were randomised to continue d4T (33) or substitute ZDV (46) or ABC (34).355 (74%) children received NVP, including 57% of those aged ≥3 years; 24% received EFV. The primary endpoint was grade 2/3/4 clinical or grade 3/4 laboratory adverse events (AEs), adjudicated by blinded endpoint review. VL was measured retrospectively on stored samples at weeks 0,48,96. Skinfold thicknesses were measured 6-monthly.

Results: 51% were boys. In naïve children, median(IQR) age at randomisation was 2.6(1.6,4.0) years; 50% had clinical Stage WHO 3/4 disease;CD4 was 20%(13,25) and VL 53,768 (23060,146132)c/ml. In experienced, median age was 6.2(5.5,7.2); CD4% 35%(30,39). Over median 120(108,132) weeks,434(91%) remained in follow-up; 25(5%) were lost/withdrew and 19(4%) died. 104(67%) d4T, 103(65%) ZDV and 105(64%)ABC children had ≥1 grade 2/3/4 AE (p=0.63). Time to first SAE (mainly hospitalisations) was also similar between groups (p=0.46). 7(4%) d4T, 13(5%) ZDV and 2(0.6%) ABC children had ≥1AE which resulted in ART being modified (p=0.01), of which 2 were attributed to d4T (both lipodystrophy in experienced children), 8 to ZDV (all haematological); no substitutions were attributed to ABC toxicity. Grade 3 or 4 anaemia/neutropenia occurred in 5/4 d4T, 9/12 ZDV and 6/5 ABC respectively (p=0.42/p=0.04). Nine children substituted drugs for TB treatment and 5 (all naïve) switched to second-line ART (1,2,2). Change in sum of 4 skinfold thickness z-score was similar across all randomised groups (p=0.62).
At week 96, VL was <100/<400c/ml in 76%/87%, 76%/77% and 84%/88% naïve children on d4T, ZDV and ABC respectively (global p=0.32/0.07). VL was <100/<400c/ml in 97%/97%, 100%/100%, and 97%/97% experienced children. CD4% changes were similar across arms (p=0.15), increasing by 16% to 36% in naïve children, and remaining stable in experienced. There were 14 new WHO 3/4 events (3 d4T, 4 ZDV, 7 ABC) and 19 naïve children died (7, 3, 9; p=0.5 for progression to WHO3/4/death).

Conclusions: NRTI-related toxicity was infrequent in African children receiving WHO-recommended dual or triple FDCs with NVP or EFV. In under 5s starting ART, there was no evidence of lipodystrophy over 2.5 years of d4T; haematological events were slightly higher in ZDV vs other NRTIs, although substitutions were more frequent; no child had ABC hypersensitivity. VL and CD4 responses were excellent, sustained and similar between randomised arms.

6th International Workshop on HIV Pediatrics

Abstracts
Poster presentations

Abstract: P_01

Treatment of pediatric HIV infection

Long term immunity of one-dose immunization with Neisseria meningitidis C conjugated vaccine, and response to re-immunization among HIV-vertically infected children

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Background: In Brazil, since 2007 all HIV infected children have been immunized with one dose of *Neisseria meningitidis* C conjugated vaccine(MCC) free of charge. The aim of this study is to describe the long term immune response (LTR) to MCC, and their response after re-imunization (RR).

Methods: HIV-infected patients, aged 2-18 years old, with CD4+ cell > 15% or 350 cell/mm^3, without active infection or opportunistic disease, without antibiotic use, were enrolled. Protective antibody titer was defined as a serum bactericidal antibody ≥ 1:4 (with human complement), and seroconversion was defined as 4-fold increase in post-immunization hSBA titer. Patients were evaluated during the immunization, 1-2 months after for seroconversion, 12-18 months for LTR and re-immunization, and 1-2 months after the re-immunization to evaluate RR. Bivariate analysis were performed, and variables with p-value <0.15 were independently evaluated through logistic regression analysis.

Results: 58 children were enrolled. Median age was 12 years. 24 (41.3%) were female, 33 (56.9%) had a history of at least one C clinical category (CDC) event, 26 (44.8%) seroconverted 1-2 months after the immunization. 18 (31.0%) presented mild adverse events, and they were not more frequent among the children who seroconverted. 16 (27.6%) presented LTR, and 47 (83.9%) had protective antibody after the re-immunization. Factors associated with LTR were: hSBA pre-immunization ≥ 4 (OR= 12.2, 95%CI= 1.3-113.3); undetectable viral load at time of immunization (OR=7.5, 95%CI= 1.2-48.5), and nadir of CD8+ lymphocytes percent (OR=1.1, OR=95%1.0-1.1). Factors associated with RR were: undetectable viral load at time of immunization (OR=4.3, 95%CI= 0.9-21.2) and seroconversion after the first dose of the vaccine (OR=6.8, 95%CI= 0.8-61.9).

Conclusion: In HIV-vertically infected children, two doses of MCC are necessary to reach the same seroconversion rate as the general population. Although the LTR was low, they presented a good RR, indicating that the vaccine induced the development of immunological memory. Undetectable viral load is the most consistent factor associated with LTR and RR. Baseline factors such as higher CD8+ lymphocytes nadir and hSBA pre-immunization titers are associated with LTR.

No conflict of interest

Abstract: P_02

Treatment of pediatric HIV infection

Self-Reported experience with financial incentives for virologic suppression among HIV-infected pediatric patients and their guardians

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Introduction: One component of the HPTN 065 (Test, Link to Care Plus Treat) study randomized study sites to evaluate the effect of financial incentives (FIs) on viral suppression. Children's National Hospital was randomized to provide quarterly $70 FIs for patients on antiretroviral therapy (ART) with HIV RNA <400 copies/mL. We assessed adolescent and guardian self-reported perceptions of the FIs.

Material & Methods: Adolescents and guardians of pediatric and adolescent patients who received FIs were invited to participate in a survey within 6 months of last FI: guardians only for patients <12 years of age, and patients, guardians or both for adolescents aged 12-20 years. Surveys focused on experience with the FIs and perception of the FI effect on adherence and laboratory results using a Likert Scale. Descriptive statistics were used to analyze results.

Results: Of 146 eligible patient/guardian pairs, 119 were enrolled. The guardian (57) adolescent (34) or both (28) completed the survey, for a total of 62 adolescents and 85 guardians. The majority of adolescents (85%; n=53) and guardians (92%; n=78) were very or extremely satisfied with receiving FIs. The majority of adolescents (69%; n=43) and guardians (67%; n=57) reported that FIs 'encouraged them/their child to take medicines'. More than half of the adolescents (55%; n=34) and 46% of the guardians (n=39) reported that the FIs helped them to be 'more informed about their treatment results'. An equal proportion (44%) of the adolescents (n=27) and guardians (n=37) believed that 'their/their child's laboratory values improved because of the FIs'. Only 10% of the adolescents (n=6) and guardians (n=8) reported that they/their child will be less likely to take their medicines after discontinuation of FIs.

Conclusions: The majority of the adolescents and the guardians of children and adolescents reported positive experiences with the FIs and believed that the FIs helped adherence and encouraged knowledge of laboratory results. However, only 44% of patients and guardians believed that the FIs helped improve laboratory values. Examination of the effect of FIs on viral suppression in the overall study is ongoing.

No conflict of interest

Abstract: P_03

Treatment of pediatric HIV infection

The 10-year Effectiveness of Highly Active Antiretroviral Treatment in Perinatally HIV-infected Children Participating in Thailand's National Access Program

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Background: From August 2002 to July 2003, 107 HIV-infected antiretroviral-naive severely-immunosuppressed children were initiated on highly active antiretroviral treatment (HAART) under the National Program for Access to Antiretroviral Treatment at Chiang Mai University Hospital. Generic drugs and/or adult formulations of the first-line non-nucleoside reverse transcriptase inhibitors(NNRTI)-based regimen, consisting of lamivudine, stavudine, and either nevirapine or efavirenz, were used. This study aimed to determine long-term effectiveness of HAART.

Methods: Demographic characteristics, clinical and laboratory data were extracted from medical records. Primary endpoint were proportion of children remained on the first-line HAART regimen, and children with plasma HIV RNA level(pVL) <50 copies/mL at week 520. Secondary endpoints were current CD4 lymphocyte count and percentage, weight-for-age (WAZ) and height-for-age (HAZ) z-scores, final height at age ≥ 18 years, education/job status, and incidence of hypercholesterolemia (cholesterol>200 mg/dl), or hypertriglyceridemia (triglyceride>200 mg/dl).

Results: 107 children were enrolled, at baseline their median age was 7.6 years (interquartile range, IQR5.7-10.0), the median CD4 lymphocyte count and percentage were 60 cell/mm^3(IQR21-272) and 3% (IQR1-9),

respectively; the median pVL was 5.37 log_{10} copies/mL (IQR5.01-5.76). At week 520, 6(6%) were transferred out to community hospitals, 9(8%) died from HIV-related illness, and 2(2%) were lost to follow-up. Among the 90(84%) adolescents who were actively followed, their median age was 17.8 years (IQR15.8-19.8). Fifty-two (58%) were female; four have delivered HIV-uninfected infants. Seventy-two (80%) remained on the first-line, while 18(20%) were switched to the second-line HAART regimen at the median time of 272 weeks (IQR261-404) on HAART. Sixty-nine (77%) had pVL<50 copies/mL; eighty-three (92%) had CD 4 $\geq$ 200 with the current median CD4 of 636 cells/mm^3 (IQR466-804) or 31% (IQR26-34). The mean(SD) WAZ and HAZ increased from -2.1(1.1) and -2.4(1.3) to -0.8(1.1) and -1.2(1.1), respectively (p<0.001). For those aged >18 years, the mean final height were 163 cm(SD10) for male(n=18) and 152 cm(SD5) for female(n=26). All (100%) attended school/college/vocational training or were being employed. Fifteen(17%) had hypercholesterolemia, and 15(17%) had hypertriglyceridemia; 4(4%) had both.

Conclusion: Approximately two-third of perinatally HIV-infected children who experienced severely immunosuppressed could grow up; have favorable immunologic outcome and sustainable long-term virologic control on the first-line NNRTI-based HAART.

No conflict of interest

Abstract: P_04

Treatment of pediatric HIV infection

Clinical and virological follow-up in perinatally HIV-1 infected children and adolescents from the Madrid Cohort with triple resistant viruses

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Background: Drug resistance mutations (DRM) compromise the success of present and future antiretroviral treatments (ART) in HIV-1 infected children. Although higher rates of triple-class antiretroviral drug resistance in pediatric cohorts compared to adult have been described, studies are scarce. We report the virological and clinical follow up of a Spanish Cohort of perinatally HIV-infected children and adolescents after the selection of triple resistant virus.

Methods: We identified patients from the Madrid Cohort of HIV-infected children and adolescents (n=534) carrying HIV-1 variants with resistance mutations to the three main antiretroviral families (TC-DRM): nucleoside reverse transcriptase inhibitors (NRTI), non-nucleoside reverse transcriptase inhibitors (NNRTI) and protease inhibitors (PI). We recovered *pol* sequences or available resistance profiles from each patient from 2000 to December 2011, recording epidemiological, clinical and virological data when TC-DRM according to IAS-USA 2013 guidelines was detected. Drug susceptibility was predicted using the Stanford´s HIVdb Algorithm. Evolution of viral load, CD4 counts, ART regimens and drug susceptibility were recorded from the moment of TC-DRM detection until December 2013.

Results: Viruses harboring TC-DRM were observed in 48 (9%) of the 534 children and adolescents from 2000 to 2011. Among these 48 children, 95.8% were diagnosed before 2003, 91.7% were Spaniards, 89.6% carried subtype B, nearly 60% have received mono or dual therapy as first regimen and 43.8% were transferred to adult units during the study period. When triple resistance was detected, the mean age was 10.5 years. The complete medical records of 37 patients showed ART duration for a mean of 11 years (range 2 months-20 years), with frequent regimen switches (mean 6.5, range 1-13) and drug experience (mean 9.5 drugs, range 3-18). Up to 80% had received at least one off-label drug according to European Medicines Agency. The

most common TC-DRM present in ≥50% of the 48 patients were D67NME, T215FVY and M41L for NNRTI, K103N for NNRTI and L90M and M46IL for PI. However, despite having TC-DRM, we observed a preserved susceptibility to several drugs within these three antiretroviral families. In fact, among the 30 children with available *pol* sequence, Stanford's HIVdb Algorithm predicted full susceptibility to darunavir in 20 children (66.7%), to etravirine and rilpivirine in 11 (36.7%), to tipranavir in 33.3%, to stavudine in 6 (20%), to zidovudine and tenofovir in 5 (16.7%) and to lamivudine and emtricitabine in 4 (13.3%). Three children (10%) were susceptible to nevirapine, efavirenz, saquinavir and fosamprenavir, two (6.7%) to indinavir and lopinavir and only one (3.3%) to atazanavir. All 30 children presented high resistance to didanosine, abacavir and nelfinavir. Viral load and lymphocyte counts in the last visit of the 48 children revealed that 60.4% reached <50 HIV-1-RNA copies/ml and 66.7% had >500 CD4+Tcells.

Conclusions: Despite the selection of HIV-1 resistance mutations to the three main antiretroviral families in our pediatric cohort, some drugs maintained their susceptibility, mainly the new PI (tripanavir and darunavir) and NNRTI (etravirine and rilpivirine). Data will help to improve clinical management of HIV-infected children carrying triple resistance in Spain.

No conflict of interest

Abstract: P_05

Treatment of pediatric HIV infection

Trends in pediatric characteristics at antiretroviral therapy (ART) initiation, and retention on ART in Swaziland, 2004-2010.

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Introduction: Swaziland's national antiretroviral therapy (ART) program was initiated in 2004. Adults and children initiated ART according to World Health Organization (WHO) guidelines, and, when stable (ART adherent and clinically well), were down-referred to lower-level health facilities for follow-up care.

Methods: A retrospective cohort study to assess attrition (documented death, stopping ART, loss-to-follow-up, LTFU defined as no clinic visit in >90 days) was conducted among a nationally representative sample of children initiating ART during 2004-2010. 12/28 clinics initiating children < 15 years(y) on ART were selected using probability-proportional-to-size sampling; medical records were randomly selected for abstraction. Changes in characteristics at ART initiation were assessed using trend tests. Adjusted hazard ratios, AHRs (95% Confidence Intervals) for attrition were estimated using Cox proportional hazards regression models adjusted for multistage sampling and study design.

Results: Among 2008 pediatric ART enrollees, 30% were < 2y, 20% 2-4y, 32% 5-9y and 18% 10-14y. During 2004-2010, the proportion of ART enrollees < 2y increased from 8% to 34%; the proportion with WHO stage III/IV declined from 90% to 61%; and among children ≥5y at

ART initiation, median CD4+ count increased from 199 to 267 cells/ µL. At 24 months after ART initiation, 78% remained on ART, 5% had died, and 16% were LTFU, trends over time were not statistically significant. In a complete-case multivariable analysis (N=1,275), attrition did not change with year of ART initiation. Compared with children 0-2y, children 10-14y had lower attrition: AHR 0.34(0.22-0.53). Compared with children starting ART at WHO stage I/II, children with WHO stage IV had higher attrition: AHR 1.66(1.13-2.45). For every one-unit increase in weight-for-age z-score, risk of attrition decreased 13%: AHR 0.87(0.82-0.92). Down-referral after ART initiation was protective against attrition in univariate analysis: AHR 0.43(0.23-0.82), but not in multivariable analysis: AHR 0.52(0.23-1.20).

Conclusions: Over the evaluation period, more children initiated ART at a younger age and with less advanced HIV disease. The lower attrition observed among down-referred children is likely due to selection of children with fewer risk factors for attrition, but could be a viable strategy for optimizing retention.

No conflict of interest

Abstract: P_06

Treatment of pediatric HIV infection

Trends in paediatric antiretroviral and cotrimoxazole prophylaxis coverage among the priority countries

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Introduction: Most of the HIV-infected children often present with symptoms in their first year of life and it is estimated that about one-third of the infected infants would have died by first year of life and about half by 2 years of age. Antiretroviral therapy (ART) has greatly changed the burden of HIV infection in many countries and lots of HIV-infected children now survive to adolescence and adulthood. Therefore it is important to make available antiretroviral therapy (ART) for these infants and children. Pneumocystic jirovecii pneumonia has been identified as a leading cause of death in infants with HIV infection with its peak incidence around the first six months of life. Due to the high mortality rate, cotrimoxazole was recommended for the children who are at risk of contracting it. This study is to evaluate the trend of access to antiretroviral and cotrimoxazole prophylaxis by children in the priority countries of sub-Saharan African since 2009 when the call for virtual elimination of mother-to-child-transmission (MTCT) was made.

Material and Materials: We used data from the 2013 United Nations Children's Fund (UNICEF) Children and AIDS Sixth Stocktaking Report. This was representative of the 2009 – 2012 periods in 21 priority countries of the Global Plan in Sub-Saharan Africa. We analysed the following variables: proportion of ART coverage among children less than 15 years; proportion of infants born to pregnant women living with HIV on cotrimoxazole prophylaxis; and number and proportion of infants born to pregnant women living with HIV on antiretroviral prophylaxis to prevent mother-to-child-transmission. Mean differences were compared using the paired t test, considering P-values of <0.05 statistically significant. All data processing and analyses performed using STATA version 12 software.

Results: The ART coverage among <15 years old progressed from 22% to 35%, MD 13, p=0.000. 90% (27 out of 30) of the sub-Saharan African countries had complete data for the period under review. Only 62% (13/ 21) of the priority countries had complete data for cotrimoxazole prophylaxis, with an average of 38% coverage in 2012, MD 10%, p= 0.1301. 86% (18/21) of the countries had complete data for infants born to pregnant women living with HIV started on antiretroviral prophylaxis to prevent MTCT. 556098 infants were started on ARV prophylaxis in 2012 and South Africa accounts for 43% of the total number. The average coverage among the infants that needed ARVs to prevent MTCT was 50%, Botswana and Namibia led the pack with >90% coverage while Nigeria had only 6%.

Conclusions: There was a significant progress in terms of provision of ARVs for children but it is still not enough. Cotrimoxazole prophylaxis also recorded some increase in most of the countries. There is need to investigate the reason why some countries are doing very well and others are not meeting their targets. The poor performing countries should request for technical support from international and bilateral partners in order to meet up.

No conflict of interest

Abstract: P_07

Treatment of pediatric HIV infection

Standardized determinations of causes of death among children and adolescents in the TREAT Asia Pediatric HIV Observational Database (TApHOD)

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Background: Causes of death among children and adolescents living with HIV in resource-limited settings are not reported in a standardized way. The purpose of this study was to describe specific causes of death in a regional cohort in Asia using an established methodology originally developed for adults.

Material and Methods: The study was conducted through the TREAT Asia Pediatric HIV Observational Database (TApHOD), which includes long-term follow-up data collected from 16 centers in 6 countries. Information on deaths occurring in the cohort was prospectively collected between 2008 and 2013. For each death, a standard Cause of Death (CoDe) form was completed by clinic physicians, including designations for immediate, contributing, and underlying causes of death. These forms were then reviewed by two clinicians, who independently assigned the causes of death. A final review confirming the causes of death was conducted through a central adjudication process performed by a panel of 3 clinicians. The underlying causes of death (i.e., the disease that initiated the sequence of morbid events leading to death) and associated clinical data are reported here. AIDS-related diagnoses were evaluated using WHO clinical staging criteria.

Results: Of the 4398 children and adolescents in follow-up, 258 (5.9%) died between January 2008 through 2013. For 228 (88%; 136 males, 92 females) deaths, a CoDe form was completed and submitted through the review process. Among these, the underlying causes of death for 125 (54.8%) patients were due to infections (AIDS-related: 37, 29.6%; non-AIDS-related: 88, 70.4%) and 34 (14.9%) due to non-infectious causes (AIDS-related: 16, 47.1%; non-AIDS-related: 18, 52.9%). An additional 19 (8.3%) deaths were caused by idiopathic diarrhea, 15 (6.6%) by AIDS (unspecified), and 35 (15.4%) were due to unknown causes. Overall, the most frequent non-AIDS-related causes of death were pneumonia (22.4%), sepsis (6.6%) and non-disseminated tuberculosis (5.7%). The most common AIDS-related causes were wasting (5.3%), cytomegalovirus infection (3.9%), and Pneumocystis pneumonia (3.5%). At the time of death, the median age was 4.8 years; 23.7% were below 18 months. For the 178 (67%)

tested, the median CD4% before death was 6.3% (IQR: 1.5%-17%); 43% had CD4% <5%. Overall, 78% had height-for-age z scores <-2 and 86% had weight-for-age z scores <-2. ART had been initiated in 171 (66%) children. At the last clinic visit, 160 (94%) had been on HAART for a median (IQR) duration of 4 (1-36) months; 26 had switched to second-line regimens.

Conclusion: The majority of underlying causes of death in this cohort were due to infections, with a substantial proportion due to non-AIDS-related causes. Most children were severely immunosuppressed and malnourished at the time of death. Together with a short time on HAART, this increases the possibility of immune reconstitution syndrome as a main contributor to these deaths. Our findings emphasize that earlier diagnosis and linkage to care and support for nutrition are imperative in order to reduce mortality. Standardized, pediatric-specific methods of determining causes of death in perinatally infected children and adolescents with HIV would help to target future program interventions.

No conflict of interest

Abstract: P_08

Treatment of pediatric HIV infection

The predictability of NONMEM generated clearance values of efavirenz in South African children.

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Background: There are multiple factors affecting the pharmacokinetics of efavirenz (EFV), with the influence of genetic factors becoming increasingly important. The CYP2B6 polymorphisms are significantly associated with interindividual clearance variation of EFV in the literature. This study investigated if either the *CYP2B6 516G>T* single nucleotide polymorphism (SNP) alone or a haplotype combination of the *CYP2B6 516 G>T*; *785 A>G* and *983T>C* can be used to predict clearance values of efavirenz with NONMEM (non-linear mixed-effect modeling program).

Methods: Two efavirenz blood samples were taken at mid-dose interval from HIV-infected children at 1,3,6,12,18 and 24 months post treatment initiation and were determined by a validated LC/MS/MS method (LOQ =0.094 µg/ml) . Polymerase chain reaction (PCR) was performed. Genotyping for *CYP2B6 516G>T* and *785A>G* were done by restriction fragment length polymorphism (RFLP), while primer extension mini sequencing was performed for *CYP2B6 983T>C*. The efavirenz plasma concentrations of each individual *CYP2B6* SNP (*mentioned in the study*) and inferred haplotypes were fitted by a one-compartment model with first-order absorption and elimination using NONMEM with interoccasion variability (IOV).

Results: Six-hundred forty nine (649) efavirenz plasma samples were collected from 60 children. The baseline ages ranged from 3.2 to 14.8 years (average 6.8) and 52 % were males. The haplotypes that significantly correlated with the plasma levels were *T-G-T, G-G-T* and *G-A-T* (with respect to *516G>T*, *785A>G* and *983T>C*, respectively). The covariates age, weight and genotype/haplotype were included in the model for the population estimates for CL/F with NONMEM. The CL/F values were 2.46, 4.6 and 7.33 l/h respectively for the *CYP2B6 516 T/T*, *G/T* and *G/G* genotype groups (objective function value (OFV) = 170). The Cl/F values were 3.02, 7.76, 7.88 and 4.39l/h respectively for the *T-G-T, G-G-T, G-A-T* and non-haplotype groups (OFV =176).

Conclusions: The replacement of the *CYP2B6 516G T/T, G/T* and *G/G* genotype groups with the constructed haplotypes increased the OFV by 5 units. It can be concluded that the *CYP2B6 516 G>T* polymorphism is a better indications of EFV clearance, generated by NONMEM, in our study population and can be employed in a clinical setting to improve therapeutic outcome.

No conflict of interest

Abstract: P_09

Treatment of pediatric HIV infection

Effects of ART timing and HIV progression on neuro-metabolite levels in basal ganglia at age 5 years

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Introduction: Early antiretroviral therapy (ART) improves HIV prognosis in young children, but little is known about long-term effects. Brain metabolites measured using Magnetic Resonance Spectroscopy (MRS) provide a good biomarker for studying the effects of HIV and early ART on neurodevelopment. The basal ganglia (BG) are a prime site for neurocellular activity and proliferation. This study examines metabolite level differences in BG for HIV-infected children initiating ART at different ages, and associations with clinical measures of disease progression.

Methods: Participants were 34 HIV-infected (age = 5.5 ± 0.3 yrs) and 15 HIV-uninfected (5.6 ± 0.5 yrs) IsiXhosa children from Cape Town, South Africa. HIV-infected children were from the *Children with HIV Early ART* [CHER] trial in which infants with CD4% ≥25% at median age 7 weeks were randomised into: ART-Def (ART deferred until CD4%<25% in 1st year & CD4%<20% thereafter), ART-40W (immediate ART until week 40), and ART-96W (immediate ART until week 96). ART was restarted after 40 or 96 weeks if certain clinical criteria appeared. Single voxel ^{1}H-MRS was acquired in the right BG with a real-time motion and B0 corrected point resolved spectroscopy (PRESS) sequence on a 3T Allegra MRI (Siemens, Erlangen, Germany). Processing included eddy current compensation, frequency-phase correction, and quantification of absolute metabolite levels. We assessed the neurometabolites N-acetyl-aspartate (NAA, neuronal integrity), and glycerophosphocholine + phosphocholine (GPCPCh, cellular density). We report data for 12 ART-Def, 11 ART-40W, 11 ART-96W, and 15 control children using one-way between group ANOVA, regression models to control for confounders (age, birth weight, and gender), and Pearson correlations for clinical measures.

Results: In contrast to our hypothesis, NAA was higher in infected children compared to uninfected controls (mean ± sd: HIV=5.3±0.4 mM, CTRL=5.0±0.4 mM, p = 0.02). Regression analyses reveal that while increasing age (5-6 yrs) in controls is associated with decreasing NAA (β=-0.6, p=0.02), there is a significant age by group interaction effect resulting in increasing NAA with age in the ART-Def group *only* (*slope*=0.8, p=0.008). Amongst infected children, lower CD4/CD8 ratio at enrolment is associated with lower NAA (r=0.56, p=0.001) and GPCPCh (r=0.38, p=0.03) levels at age 5.

Conclusion: Lower metabolite levels in uninfected controls compared to infected children may be due to the fact that 80% of these uninfected children had been exposed to HIV *in utero*. Noticeably, CD4 and CD8 at enrolment (median age 7 weeks) were the *only* clinical measures that predicted NAA and GPCPCh levels at ages 5-6 years amongst infected children, with more advanced disease stage in infancy correlating with lower levels at this later age, irrespective of the timing of ART initiation. These results provide support for earlier initiation of ART in infected children. The positive association between age and NAA in the ART-Def group only, suggests that delayed ART adversely affects the BG, effects that appear to be partially reversed after initiating ART. Longitudinal studies are needed to support these observed patterns, and the clinical significance of these findings require further exploration.

No conflict of interest

Abstract: P_10

Treatment of pediatric HIV infection

Raltegravir Pediatric Development: New Options for Treating the Youngest Children with HIV

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Background: In collaboration with the IMPAACT network, Merck has undertaken a comprehensive program for pediatric development of raltegravir, supported by favorable preclinical and adult clinical data, a metabolic profile with few significant drug-drug interactions, and successful pediatric formulation development.

Methods/Results: IMPAACT P1066 is a Phase I/II dose-finding and treatment study of HIV-1 infected children (either treatment-experienced or, if <6 mos, having failed PMTCT) with the primary goals of dose finding and assessment of safety at 24 weeks. P1066 used 3 raltegravir formulations: adult film-coated tablets (6-18 yrs); chewable tablets (2 to <12 yrs); and granules for oral suspension (4 wks to <2 yrs), added to an optimized background ARV regimen. 152 subjects were enrolled; PK targets were achieved using fixed dosing of the 400mg film-coated tablet (for children >25 kg) and weight-based dosing (6 mg/kg) of the chewable tablets and granules for oral suspension, all given twice daily. Acceptable safety (few drug-related (DR) AE, 1 discontinuation due to DRAE) and efficacy (HIV-RNA <400 c/mL achieved in 73.6% of subjects aged 2-18 yrs and 70% of subjects aged 4 wks to <2 yrs) were demonstrated by Week 48 for all age groups and formulations, leading to regulatory approvals in the US and elsewhere.

A separate study was planned to establish PK and safety in HIV-exposed neonates. Due to immaturity of the UGT metabolic pathway in neonates and emerging data indicating high rates of transplacental raltegravir passage in pregnant women, IMPAACT P1097 was conducted to establish the washout PK of raltegravir in neonates born to mothers receiving raltegravir in late pregnancy, before initiating an active dosing study. P1097 enrolled 22 mother-infant pairs, confirmed high rates of transplacental passage (median cord:maternal blood concentration ratio 1.48), and demonstrated highly variable and prolonged elimination of raltegravir in the first days of life ($t_{1/2}$: 26.6 hrs [range: 9.3-184 hrs]), compared with older infants and children. In addition, P1097 will enroll a new cohort of low birth weight (including premature) neonates to provide washout PK and safety data for raltegravir in this fragile subpopulation.

IMPAACT P1110 is an ongoing 2-part PK and safety study of raltegravir in term neonates at high risk of acquiring vertical HIV infection, and was informed by P1097 results. Part 1 will collect intensive PK and safety data from 2 single raltegravir doses, at birth and 7-10 days, in ~12 subjects to estimate raltegravir clearance in the first 2 wks of life. Modeling and simulation will be used to project a multiple dosing scheme to be used in Part 2 to provide continuous treatment from birth to 6 wks in 20 additional PK evaluable infants.

Conclusion: At present raltegravir offers a new class of ARV for children with HIV infection as young as 4 wks of age, with favorable safety and efficacy, and has been approved for use in 2 suitable pediatric formulations (chewable tablets and granules for oral suspension). Completion of this comprehensive program should provide data on the potential use of raltegravir spanning the entire pediatric age range, beginning at birth.

Conflict of interest : I am an employee of Merck & Co., Inc.

Abstract: P_11

Treatment of pediatric HIV infection

Virological outcomes after anti-retroviral therapy initiation among a cohort of children in Quebec, Canada

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Introduction: The first wave of HIV-infected children to be treated with optimal combination anti-retroviral therapy (cART) in the developed world setting has now reached adolescence. Little is known on the virological outcomes among this group. The objective of this study is to assess time to virological failure (VF) and treatment interruption (TI) among HIV infected children initiating treatment in the province of Quebec, Canada.

Material & Methods: Study subjects were enrolled in the Centre Maternel et Infantile sur le Sida (CMIS) cohort between 1997 and 2010. Children were followed clinically every one to three months by multidisciplinary care team comprised of pediatricians, nurses, social workers, psychologists, and pharmacists. HIV-1 plasma RNA levels were measured every three months after cART initiation using the versant HIV-1 RNA assay (Bayer, Pittsburg). Primary outcome was time to first VF, defined as detectable viremia over two consecutive measurements after an initial response to cART, and TI, defined as cessation of cART for more than 6 months at any time after initiation.

Results: Among the 174 children followed at CMIS during the entire study period, only 45 initiated cART at our center. Median follow-up time was 37.8 (IQR 19.2-59.4) months. Median time to first VF was 32 months (IQR 14-44); cumulative incidence of VF at 24, 48 and 96 months of follow-up was 28%, 51%, and 79% respectively. Median time to TI was 52.2 months (IQR 24-72 months), cumulative incidence of TI at 24, 48 and 96 months was 11.8%, 20.4% and 51.13% respectively. Girls were more likely than boys to experience a TI (HR 3.84, 95% CI 1.38-10.10). Children initiated on cART during infancy were more likely to experience VF compared to those initiating treatment after twelve months of age (HR 3.03, 95% CI 1.38-6.72). Factors not associated with either VF or TI included viral clade (B vs. non B), family structure (mono vs. bi-parental) or type of regime initiated (PI vs. NNRTI). Among all treated patients (n=108), including those receiving prior sequential mono-bi ART therapy, only 64% had achieved at least I year of sustained virological suppression at any time during their follow-up.

Conclusions: In this cohort of HIV infected children initiating cART in Canada with close monitoring, in the care of a multi-disciplinary care team, under a system of universal health care access, over 50% experienced VF within 4 years of cART initiation, and over 50% had a TI at some point during their follow-up. These results are concerning given recommendations for life-long therapy in children, and the limited therapeutic options available.

No conflict of interest

Abstract: P_12

Treatment of pediatric HIV infection

Anemia and effect of iron supplementation among HIV-infected children in India

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Background: Anemia in pediatric HIV is poorly studied in India. We examined prevalence and etiology of anemia among children with

perinatally acquired HIV infection in a non-malaria endemic region, and assessed effect of iron supplementation on growth and clinical status.

Materials and methods: Between Feb 2010-Aug 2011, 240 eligible HIV-infected children aged 2-12 years were recruited at 3 sites in 2 high HIV-prevalence states in South India. Definitions were as follows: anemia: age<5yrs: Hb<11gm/dl; 5-12yrs: Hb<11.5gm/dl; iron deficiency: serum transferrin receptor (sTfR)-ferritin index ≥0.75; and anemia of inflammation (AI): sTfR/ferritin≤0.75 + CRP<1.0mg/dl. Anemic children were given iron supplementation (3gm/kg/day). Children were followed every 3 months for 1 year.

Results: Mean age was 7.7years (±2.6), 131 were males (54.6%), 19.2% were in WHO clinical stage 3 or 4, with median CD4 count 25% (IQR=18, 33). Prevalence of stunting was 40.0%; underweight was 45.4%, intestinal parasitic infestation was 13%, and 104/240 (43.3%) were on ART at baseline. Baseline prevalence of anemia was 46.7%. Significant independent risk factors for anemia were age (RR 2.9, 95%CI 1.3-6.4) underweight status (RR 2.0, 95%CI 1.1-3.8), CD4 <25% (RR 3.5, 95%CI 1.8-6.7) and non-ART status (RR3.1, 95%CI 1.3-7.2). Iron deficiency, chronic inflammation and vitamin A deficiency emerged as main etiological factors for anemia. Iron supplementation was associated with median Hb increase (10.4gm/dl to 11.3mg/dl, p=0.003) and iron deficiency prevalence decrease (90% to 79%), and mild adverse effects (24%). Beneficial effects were enhanced in the presence of ART. Growth rate, hospitalization and incidence of illness were similar in both groups.

Conclusions: HIV-infected children had a high prevalence of anemia attributable to iron, vitamin A deficiency and chronic inflammation. Anemia responded well to iron supplementation, particularly when used along with ART.

No conflict of interest

Abstract: P_13

Treatment of pediatric HIV infection

A 24 week analysis comparing virological suppression in early vs. delayed initiation of ART in HIV-infected children with Severe Acute Malnutrition (SAM)

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Introduction: Malnutrition is a common presenting clinical problem in HIV-infected children in developing countries; up to one third of children treated for severe acute malnutrition (SAM) in Sub-Saharan Africa are HIV positive. The World Health Organization (WHO) has highlighted research into the optimal timing of ART in children with SAM as a priority. The initiation of ART in malnourished children is associated with higher mortality and delayed immunological recovery compared to non-malnourished children. The reasons for these findings are poorly understood, but may be related to poor absorption of antiretroviral therapy during the acute phase of malnutrition.

Materials and Methods: This is a prospective, randomized controlled interventional trial comparing initiation of ART within 7 days of admission to hospital (early arm), to delaying initiation until recovery from the acute phase of severe malnutrition to a maximum 21 days from admission (delayed arm). All patients were managed as per the 'WHO Guidelines for the inpatient treatment of severely malnourished children' at King Edward VIII Hospital, Durban, South Africa. HIV RNA Viral loads were performed at baseline, 4 wks, 8 wks, 12 wks and 24 wks. Virological failure was defined as a HIV RNA Viral load > 1000 copies/ml at 24 weeks.

Results: The interim analysis was performed at 50% of the target recruitment (37/75 subjects). The cohort was 51% female with an age range of 2months – 10years. The average age of patients <2 years (n=27) was 10 months

and >2yrs (n=10) was 4.6 years. The mortality was 12.3% in the early arm (n=2) and 15% in the delayed arm (n=3) (p=0.41). 22 patients completed 24weeks follow-up on the study, 10 in the delayed arm and 11 in the early arm. Analysis of HIV viral loads at 24 weeks revealed that 20% (2/10) of patients in the delayed arm displayed treatment failure compared to 54% (6/11) in the early arm.

Conclusions: In this interim analysis there was no difference in the mortality between early vs delayed initiation of ART in children with SAM. Patients in the delayed arm had a trend towards better virological responses at 24wks compared to the early arm. Analysis of pharmacokinetic levels of antiretroviral drugs in the early and delayed arms is planned. Delaying initiation of ART until after nutritional recovery was safe and not associated with excess mortality but was associated with a trend towards improved virological responses.

No conflict of interest

Abstract: P_14

Treatment of pediatric HIV infection

Results of the Introduction of a Hospital-based Pediatric Provider-Initiated HIV Testing & Counseling Program in Vietnam

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Background: Failure to diagnose and enroll HIV-infected children into treatment represent two major challenges to bridging the global pediatric HIV treatment gap. Provider-initiated testing and counseling (PITC) can improve identification of HIV-infected patients in need of treatment. We describe the implementation and results of a pediatric PITC program in Vietnam.

Description: The program was initiated in March/2013 at Ho Chi Minh City Pediatric Hospital #2. Health care workers from 7 departments received training on pediatric HIV symptoms and diagnosis; counseling skills; and referral procedures to pediatric HIV outpatient clinic (OPC). Additionally, a coordinator was hired to facilitate testing and OPC referrals. Impact was measured by comparing testing patterns, referral success, and referral time for 7-month periods before and after program introduction. Characteristics of children who received HIV testing pre- and post-PITC were reviewed, as well as in a random sample of 1500 inpatients (5% of admissions) from the PITC departments during the post-training period.

Lessons Learned: Lower testing was observed after the introduction of PITC (935, 1.6%) in comparison to the pre-PITC period (935, 2.8%). However, positive rate remained almost unchanged between pre-PITC (29, 3.1%) and post-PITC groups (16, 3.2%). Successful referral to OPC saw a significant improvement, increasing from 24% in pre-PITC period to 88% after the introduction of PITC. Median OPC referral time was reduced by half down to 7 days from 11 days before PITC. Common symptoms prompting testing among the 498 post-PITC patients included: pneumonia (24%), fever (22%), hematologic symptoms (22%), malignancy (13%), and other infections (10%); diarrhea (4%), and malnutrition, thrush and tuberculosis (1% each) were infrequent indications. Symptoms of PITC-identified HIV patients included: pneumonia (7, 44%), and HIV exposure, and hematologic symptoms (2 each, 13%). Possible missed opportunities for testing were identified in 91 (6%) of the 1500 untested patients. Possible testing indications included: malnutrition (31; 2.1% of admissions), pneumonia (24; 1.5%), diarrhea (10; 0.7%), and developmental delay (7; 0.5%).

Conclusions: While testing decreased and accuracy of identifying HIV-infected children remained unchanged, referral success and referral time improved post-PITC. Further study is needed to understand the decreased testing rate and increase in age of patients tested.

No conflict of interest

Abstract: P_15

Treatment of pediatric HIV infection

Prevalence and determinants of virological failure among children on antiretroviral therapy in Kenya

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Background: The goal of antiretroviral therapy (ART) is to achieve durable viral suppression. In sub-Saharan Africa, access to viral load (VL) monitoring remains limited despite reports of low virologic suppression among children. We assessed prevalence of virologic failure (VF) among children on ART in Kenya.

Materials & Methods: We conducted a sub-analysis of data on children aged 0-14 years on ART for ≥6 months enrolled consecutively in a cross-sectional study validating DBS for VL measurement in 12 purposively selected clinics. We assessed the proportion of children with VF (VL≥1000 copies/mL) and compared VF among those with indication for VL testing (clinical disease progression or inadequate immunologic response to ART) with those without indication. We used SAS version 9.4 to compute frequencies, proportions, median with interquartile range (IQR), and logistic regression to assess factors associated with VF.

Results: A total of 350 children (48.3% female) were included in the analysis; median (IQR) age was 6.6 years (3.8-9.0) and duration on ART was 40.9 months (24.3-60.0). The majority [286 (82.7%)] of the children were on a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen while 51 (14.7%) were on a protease inhibitor (PI)-based regimen. Sixty-three (18.0%) had indication for VL testing. Overall, 122 (34.8%) of children had VF; 30 (47.6%) among those with indication for VL testing and 92 (32.1%) among those without indication. Factors associated with VF were (OR, 95% Confidence Interval): male gender (1.8, 1.1-3.0), age <5 years (2.3, 1.2-4.3) relative to children age 5-10 years, having indication (2.0, 1.1-3.7), and NNRTI-based regimen (4.0, 1.8-9.0). Duration on ART was not associated with VF. A separate analysis found no difference in VF-risk between Efavirenz- and Nevirapine-based regimens.

Conclusion: We found high VF among children on ART even among those without indication for VL. This study validates the need to strengthen pediatric ART monitoring and adherence support, including prioritizing VL to avoid unnecessary treatment changes and identify VF among children without indications High VF-risk among children on NNRTI-based regimens supports the need to implement recent World Health Organization recommendations to use PI-based first line regimens for younger children to optimize virological suppression and minimize drug resistance.

No conflict of interest

Abstract: P_16

Comprehensive Pediatric HIV care

Retention of HIV Infected Children on Treatment in Uganda over 24 months following ART initiation

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Background: Paediatric ART coverage in Uganda remains low with only 30% of eligible children on treatment by the end of the 2012. However even after initiation of therapy, there is limited data on retention of these children on treatment. To establish retention rates and better characterize factors associated with loss to follow up after initiation of ART we conducted a programme assessment of the Pediatric HIV/AIDs services in Uganda.

Methods: This was a cross-sectional assessment done in the setting of the annual National Paediatric HIV services technical support supervision and monitoring activities. A total of 66 health facilities were visited across the country. Pre-designed chart abstraction forms were used to collect patient related data from patients' HIV care cards. The study population included children (0-14 years) that had been initiated on ART in the periods; April-June 2011, April-June 2012 and October-December 2012. Determination of retention on treatment was done by verifying patient treatment status as of April-June 2013.

Results: A total of 243 (M=48%, F=52%), 370 (M=44%, F=56%) and 332 (M=49%, F=51%) records were reviewed for the 6, 12 and 24 month cohorts respectively. The proportion of children retained at the initiating health facility was 80%, 79% and 67% for the 6, 12 and 24 month cohorts respectively. Overall, a higher proportion of children were retained at lower level health facilities as compared to hospitals. On bivariate analysis, factors associated with loss to follow included late initiation on ART (WHO Stage III & IV), initiation of treatment at hospital level and initiation of ART at an age ≥ 1 year; in the 6, 12 and 24 months cohorts respectively.

Conclusions: Overall retention on treatment was sub-optimal across the 24 months of observation with at least 20% of children lost by 6 months and 33% by 24 months. Early initiation of ART in children as recommended by WHO and National policy is critical. Operationalization of strategies like family clinic days, appointment books, community linkage facilitators and telephone calls can ensure that children are retained on treatment.

No conflict of interest

Abstract: P_17

Comprehensive Pediatric HIV care

CD4+ cell decline and time to reaching ART eligibility in HIV-positive children 5-14 years of age in Ethiopia and Rwanda

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Background: Absolute CD4+ cell count is a good prognostic indicator of short term risk of disease progression in adults and children ≥5years. The WHO recommends the same guidelines for initiating antiretroviral therapy (ART) using CD4+ thresholds for adults and children ≥5. Few data are available on CD4+ decline in ART-naïve HIV-infected children in Africa. We analyzed the rate of CD4+ decline in ART-naïve children 5-14years enrolled in care in Ethiopia and Rwanda, and assessed time to reaching ART eligibility per 2010 and 2013 WHO guidelines.

Methods: Using routine data, we examined CD4+ decline prior to ART initiation in HIV+ children 5-14years with CD4+≥600 cells/ml at entry to care (2004-2012) at 37 Ethiopian and 39 Rwandan health facilities supported by ICAP-Columbia University. CD4+ decline in the first 24 months was estimated using mixed linear regression modeling. Competing risk estimators were used to assess time to reaching ART eligibility at CD4+≤350 or CD4+≤500, accounting for death and ART initiation as competing risks.

Results: We analyzed 1,225 children, median age 7.3years: 74.5% 5-9years and 25.5% 10-14years. Median and mean CD4+ at enrollment were 980.0 and 887.0 [range: 601-2980] and were significantly higher among children 5-9years ($p<0.001$). Average CD4+ decline over 24 months was 8.3 cells/month

(95%CI:7.4-9.2) and 100.2 cells/year (95%CI:89.7-110.6). No significant difference was observed in rate of CD4+ decline by country or enrollment WHO stage, however age <10years was associated with more rapid CD4+ decline (p=0.05) adjusting for enrollment CD4+. By 12 and 24 months, 6.7%(95%CI:5.4-8.3%) and 15.2%(95%CI:12.9-17.7) of children reached CD4+≤350, and 16.9%(95%CI:14.7-19.1%) and 34.9(95%CI:31.8-38.0) reached CD4≤+500. Despite CD4+ differences at enrollment, no differences in incidence of reaching eligibility for ages 5-9 and 10-14years were detected.

Conclusions: In this cohort of ART-naïve HIV+ children from Ethiopia and Rwanda with CD4+ ≥600, average CD4+ decline was 100.2 cells/year – a higher rate than found in adults (roughly 60 cells/year) – and appeared to be more rapid in younger children. Only a third of patients 5-14years with CD4+ ≥600 at enrollment reached ART eligibility within 24 months using current WHO guidelines of CD4+≤500 and 15% reached CD4+≤350 cells as per 2010 WHO guidelines.

No conflict of interest

Abstract: P_18

Comprehensive Pediatric HIV care

Advanced disease among HIV-infected children eligible for antiretroviral therapy (ART) in Eastern Cape, South Africa

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Background: In South Africa in 2012, 83% of HIV-infected (HIV+) pregnant women received antiretrovirals and 63% of the 220,000 eligible HIV+ children received ART; all children < 5 years and children ≥5 years with CD4+ counts <500cells/mm^3 or WHO stage 3 or 4 were ART-eligible. Despite widespread roll-out and availability of ART, many eligible children may not receive ART which may contribute to morbidity and mortality.

Methods: ART-eligible children 0-12 years at five health facilities in the Eastern Cape, South Africa were enrolled in the Pediatric Enhanced Surveillance Study (PESS), an on-going prospective cohort study. Laboratory and clinical/behavioral/social assessments are done quarterly. We describe characteristics of enrolled children.

Results: Between April 2012 and December 2013, 272 ART-eligible children were enrolled; 100 (36.8%) <12 months, 75 (27.6%) 1-4years, 97 (35.7%) 5-12yrs. Among children <12months at enrollment, 86.0% were diagnosed before 6 months of age, 41.0% were hospitalized at enrollment, 18.0% had prior hospitalization, 15.0% had tuberculosis (TB) at enrollment and 18.0% had a history of TB; median HIV-RNA (VL) and CD4$^+$ percent (CD4+%) were 1,338,597 copies/ml (range: 12,215-10,000,000) and 21.0% (range: 2.1-67.0), respectively. In children 1-4 years, 33.3% were hospitalized at study enrollment, 38.7% had prior hospitalization, 18.7% had TB, 37.3% had TB history; median VL and CD4$^+$% were 369,697 copies/ml (range: 7,679-10,000,000) and 18.7% (range: 1.8-78.9), respectively. Among children 5-12 years, 53% were not diagnosed until ≥5yrs of age, median age at HIV diagnosis was 7.2 years and the median time from HIV diagnosis to being identified as ART eligible was 56 days (range: 1day-10 years). At enrollment among children 5-12 years, 22.7% were hospitalized and 37.1% had prior hospitalization; 21.6% had TB and 54.6% had TB history; median VL and CD4$^+$ count were: 119,194 copies/ml (range: 2,244-8,812,447) and 332 cells/mm^3 (range: 2-1478). Among 266 children with >3 months (range: 3-15 months) of follow-up, 204 (76.7%) started ART.

Conclusions: Infants and children enrolling in PESS were not detected as HIV+ until they had advanced disease, despite high rates of prior TB and hospitalizations. Delays in ART initiation also persisted for children meeting

eligibility criteria despite broad treatment availability.

No conflict of interest

Abstract: P_19

Comprehensive Pediatric HIV care

Developmental disabilities and behavioral challenges among HIV+ children in Eastern Cape, South Africa

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Background: Data on neurodevelopmental and behavioral problems in children with HIV-infection (HIV+) living in low- and middle-income countries are limited. We conducted screening for neurodevelopmental and behavioral problems using simple questionnaires in a cohort of HIV+ children eligible for antiretroviral therapy (ART) in South Africa.

Methods: ART-eligible children 0-12 years at five health facilities in the Eastern Cape, South Africa were enrolled in the Pediatric Enhanced Surveillance Study (PESS), an on-going prospective cohort study. Children 2 years and older were assessed for developmental disabilities and behavioral problems using two locally validated screening tools: the Ten Questions Screen (TQS) (children 2-9 years) and the Strengths and Difficulties Questionnaire (SDQ) (≥4 years). Both tools are based on caregiver reports and have been translated into the local language.

Results: Among 272 children enrolled as of December 2013, 154 (57%) were >2 years or older, 107 (39%) were ≥4 years and 87% and 92%, respectively, had initiated ART. Of the 85 children 2- 9 years (median: 5.6years) with TQS results, 50 (60%) caregivers reported one, 29 (35%) reported two and 12 (14%) reported three or more developmental difficulties; 16% were delays in walking and 13% were difficulty hearing. Among 66 children ≥3 -9 years in this group, caregivers reported 33% with abnormal speech, 20% not able to understand instructions and 15% not able to learn as similarly-aged children. Caregivers reported 9 (11%) children to have had seizure-like episodes. Of the 95 children 4-12years (median: 8.5years) with SDQ results, 22 (33%) caregivers reported ≥ 1 abnormal score: 14 (15%) on emotional symptoms scale, 19 (20%) on conduct problem scale, 4 (4%) on hyperactivity scale, 20 (21%) on peer problems scale, and 6 (6%) on the prosocial scale.

Conclusions: These screening questionnaires identified a subset of HIV-positive children who might benefit from formal diagnostic evaluations to further select those who would benefit from appropriate interventions to ameliorate possible developmental delays or behavioral problems.

No conflict of interest

Abstract: P_20

Comprehensive Pediatric HIV care

Prevalence and Incidence of Liver Dysfunction in Asian Children with Human Immunodeficiency Virus

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Background: Data that define the burden of liver disease in HIV-infected children are scarce. We determined the prevalence of liver dysfunction prior to and incidence of liver dysfunction after combination antiretroviral therapy (cART) initiation in the TREAT Asia Pediatric HIV observational database (TApHOD).

Methodology: Data from HIV-infected children aged between 2-18 years at the time of cART initiation who had baseline alanine aminotransferase (ALT) within 6 months prior to cART initiation and followed at 18 hospitals in 6 Asian countries during 2008-2p2 were analysed. Prevalence and incidence of liver dysfunction were calculated. Biomarkers including aspartate aminotransferase (AST) to platelet ratio index (APRI) and FIB4 index were assessed. Using the cut-off adopted from other pediatric studies or extrapolated from adult studies, APRI scores >1.5 was suggestive of liver fibrosis, and FIB4 index scores >1.3 was predictive of possible cirrhosis. The first abnormal values detected after cART initiation were referred to as the end points.

Results: A total of 1,930 children were included. The median age was 6.9 years (interquartile range, IQR 4.5-9.4), 49% were male, and 98% were perinatally infected. Prior to cART initiation, median CD4 count was 171 cells/mm^3 (IQR 41-389); 61% had HIV RNA ≥5.0 $\log_{10}$ copies/mL, and 58% were in WHO stage 3 or 4. 4% of children had hemoglobin (Hb) level <7.5 g/dL prior to cART; 24 of 506 (4.7%) and 15 of 423 (3.5%) tested were HBsAg and anti-HCV positive, respectively.
Prior to cART, the prevalence of ALT ≥ 5 times the upper limit of normal (*ULN) was 1.9%. The median APRI score was 0.34(IQR 0.18-0.63); 8.5% of children had APRI scores >1.5, while FIB4 index scores >1.3 were found in 2.7%. The cART regimens initiated were NVP-, EFV-, and PI-based in 62%, 32%, and 6%, respectively. Only 1143 cases with normal baseline ALT (≥1*ULN) were included in the incidence analysis.
The incidence of ALT 5*ULN after cART was 0.40/ 1,000 person-months (PM) (95% CI 0.27-0.61). The incidence of APRI scores >1.5, and FIB4 index scores >1.3 after cART were 0.77/1,000 PM, and 0.63/1,000 PM, respectively. Two (0.2%) met Hy's law, defined as ALT >3*ULN and total bilirubin >2*ULN. By multivariate analysis, severe anemia (Hb <7.5 g/dL) prior to cART (HR 2.96, 95% CI 1.22-7.18, p=0.02) was a predictor of ALT ≥3*ULN or ≥3 times the baseline level, while age 5-9 years was a protective factor (HR 0.48, 95%CI 0.27-0.84, p=0.01).
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Conclusions: We demonstrated a low prevalence and incidence of liver dysfunction before and after cART initiation. Continuous monitoring during cART is required; children with liver dysfunction and/or abnormal biomarkers should be closely followed, and those with persistent abnormalities might be targeted for further evaluation of liver pathology.

No conflict of interest

Abstract: P_21

Comprehensive Pediatric HIV care

Immunity to Childhood Vaccination among HIV infected and HIV exposed children in Latin America and the Caribbean

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Background: Perinatally HIV-infected children (PHIV) are at risk of poor coverage and response to childhood vaccines. The study objective was to compare immune response to routine childhood vaccinations between PHIV and HIV-exposed uninfected (HEU) children in Latin America and the Caribbean among children who were fully vaccinated prior to four years of age.

Methods: The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development International Site Development Initiative (NISDI) enrolled PHIV and HEU children into two prospective cohort studies conducted at fifteen sites in Latin America and the Caribbean, from 2002 to 2009. Full vaccination for the different vaccines at age four was defined as three doses of hepatitis B vaccine (HBV); four doses of any tetanus toxoid-containing vaccine; three doses of *Haemophilus influenzae* serotype b (Hib) vaccine prior to 12 months of age or at least one dose of Hib given ≥ 12 months; one dose of measles-containing vaccine; and one dose of rubella-containing vaccine. Furthermore, vaccine doses must have been given at appropriate ages and intervals. Serum specimens from the four-year study visit were tested for immunity, defined as: hepatitis B surface antibody titer ≥10 IU/L; tetanus antibody titer ≥0.1 IU/mL; Hib antibody titer ≥1.0 µg/mL; measles antibody titer ≥0.120 IU/mL; and rubella antibody titer ≥10 IU/mL. Categorical variables were compared using Fisher's exact test and continuous variables by t-test.

Results: Among 442 children enrolled and followed to four years (up to 51 months), 191 had serum specimens available at that time, including 54 HEU and 137 PHIV. HEU children were significantly ($p<0.01$) more likely than PHIV children to be fully vaccinated at four years of age for tetanus (77.8% vs. 55.5%), measles (94.4% vs. 70.1%) and rubella (94.4% vs. 70.1%). Subsequent comparisons are restricted to those who were fully vaccinated. Immunity was significantly higher among HEU than PHIV children ($p<0.04$) for all vaccines examined. All HEU children (51) but only 80.2% (77/96) of PHIV children were immune to measles ($p<0.001$) (odds ratio [OR] undefined). Compared to PHIV children, HEU children were more likely to be immune to Hib (68.8% vs 51.4%; OR=2.1, 95% confidence interval [CI]: 1.0-4.3), hepatitis B (37.8% vs 20.9%; OR=2.3, 95% CI: 1.1-4.9), tetanus (90.5% vs 72.0%; OR=3.7, 95% CI: 1.2-11.6) and rubella (98.0% vs 72.9%; OR=18.6, 95% CI: 2.4-141.4). Among PHIV children, CD4% and VL at the 4-year visit (<1000 vs ≥1000 copies/mL) were not associated with immunity to most vaccines; those with VL<1000 copies/mL were more likely to be immune to tetanus ($p<0.01$). Children who started HAART prior to 12 months of age were significantly more likely to be immune to hepatitis B ($p=0.049$) compared to those on HAART >12 months and no HAART.

Conclusions: PHIV children continue to be under-vaccinated for tetanus, measles, and rubella compared to HEU children at four years of age. Once fully vaccinated, significantly lower proportions of PHIV children are immune to vaccine-preventable diseases. Strategies to increase PHIV immunity following vaccination and to improve routine PHIV vaccine coverage require further study.

No conflict of interest

Abstract: P_22

Comprehensive Pediatric HIV care

Factors Associated with Antiretroviral Therapy Adherence in HIV-Infected Children in Western Kenya

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Introduction: Factors impacting children's adherence to antiretroviral therapy (ART) in

resource-limited settings are poorly understood. We sought to better understand factors associated with adherence as measured by electronic dose monitoring in a cohort of children in Kenya.

Methods: We used Medication Event Monitoring Systems (MEMS®, AARDEX, Inc.) that record the time and date of medication bottle openings to measure ART adherence for 6 months among 191 HIV-infected children aged 0 to 14 years within a large HIV care program in Kenya. MEMS were used with bottles containing either once-daily efavirenz (EFV) or twice-daily nevirapine (NVP). At 6 time points (approximately 1 month apart), caregivers of enrolled children were asked questions about demographic, socioeconomic, and clinical characteristics of the child, caregiver, and household. Univariate analyses using Student t and Pearson Chi-square tests were performed at each time point to investigate factors associated with MEMS adherence, categorized as 'high' (90-100% doses taken), 'medium' (80-89%), 'low' (70-79%), and 'very low' (<70%). Variables significant in univariate analyses ($p<.05$) were included in multivariate ordinal logistic regression models at each time point using a backwards selection method with a p-value <.10 for variable exit selection and high MEMS adherence as the referent group. Repeated measures logistic regression using the generalized estimating equations (GEE) method was conducted to investigate factors across time points. Odds ratios (OR) with 95% confidence intervals (95%CI) are reported, and were averaged for factors significant at more than 1 time point.

Results: Fifty-six percent of child participants were female, with mean age at enrollment of 8.2 years. Median CD4 percentage was 26% and median time on ART was 2.3 years. Median adherence by MEMS was 96% and improved over the course of the study; 24% of children had very low MEMS adherence (<70%) at month 1 compared to only 9% at month 6. Factors significantly associated with lower levels of MEMS adherence in multivariate regression at only 1 time point included: child being female (OR 2.3, 95%CI 1.1-4.7), having WHO disease stage of 3 or 4 (OR 2.5, 95%CI 1.2-5.2), and knowing his/her HIV status (OR 3.1, 95%CI 1.1-8.6); caregiver being the mother (OR 2.2, 95%CI 1.2-4.0); and, the household not having in-home piped water (OR 2.1, 95%CI 1.1-3.7). Significant factors at 2 time points included: child's younger age (OR 1.2, 95%CI 1.1-1.4), and the caregiver reporting times when there was not enough food in the past month (OR 2.6, 95%CI 1.4-4.8), being employed outside the household (OR 2.6, 95%CI 1.3-5.1), and having difficulties giving the child ART (OR 2.8, 95%CI 1.5-5.2). No factors were significant at 3 or more time points. In repeated measures logistic regression, the caregiver reporting lack of food (OR 1.4, 95%CI 1.1-2.0), being employed (OR 1.6, 95%CI 1.2-2.2), and having difficulties giving ART (OR 1.7, 95%CI 1.3-2.3) were significantly associated with lower levels of MEMS adherence.

Conclusion: Child, caregiver, and household-level factors were related to adherence to ART but were not consistent across the study period, suggesting factors impacting adherence are dynamic.

No conflict of interest

Abstract: P_23

Comprehensive Pediatric HIV care

Performance of Caregiver-Reported Adherence to Antiretroviral Therapy Compared to Electronic Dose Monitoring among HIV-Infected Children in Kenya

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Introduction: Caregiver reports are widely used to assess adherence to antiretroviral therapy (ART) for young HIV-infected children, particularly in resource-limited settings, but

their validity and factors that impact their accuracy are not well known.

Methods: We conducted a 6-month prospective cohort study among 191 caregiver-child dyads enrolled in a large HIV treatment program in western Kenya. Six assessments were conducted (approximately 1 per month) with caregivers of HIV-infected children ages 0-14 years. Caregivers were asked to report the number of doses of ART the child had missed in the past 30 days. Electronic dose monitoring using Medication Event Monitoring System (MEMS®, AARDEX, Inc.) bottle caps were used as the reference standard, and each study participant was issued a MEMS cap at study initiation. MEMS were used with medication bottles containing either once-daily efavirenz (EFV) or twice-daily nevirapine (NVP). Receiver operating characteristic (ROC) curves were used to assess the diagnostic value of caregiver reports for detecting non-adherence among children as defined by MEMS. Sensitivity analyses were conducted by defining MEMS non-adherence at 3 different thresholds (<100% doses taken, <90%, and <80%). We also calculated 'agreement' between caregiver report and MEMS (i.e., both measures indicated missed doses or both indicated no missed doses). Univariate analyses and multivariate logistic regression using a backwards selection method with a p-value of <.10 for variable exit selection were performed to investigate associations between agreement and demographic, socioeconomic, and clinical characteristics of study participants at each assessment time point.

Results: Mean age of child participants was 8.2 years and 56% were female. The majority of caregivers were the biological mother of the child (62%). Caregivers reported significantly higher rates of adherence compared to MEMS; over 6 months, caregivers reported 'no missed doses' for 83% of children, while MEMS revealed no missed doses for only 36%. Caregiver reports had low sensitivity and high specificity in identifying non-adherence as defined by MEMS. Sensitivity across the 6 assessments ranged from 0.19 to 0.52, and specificity from 0.86 to 1. The area under the curve revealed low diagnostic test performance, with C-statistics ranging from 0.60 to 0.62. Agreement between measures was poor but improved over the course of the study; agreement between measures at month 1 was only 38% but at month 6 was 56%. Several factors were associated with agreement between measures in multivariate logistic regression, including child's younger age (OR 1.3, 95%CI 1.1-1.6), longer time on ART (OR 1.2, 95%CI 1.0-1.5), child having no medication side effects (OR 5.1, 95%CI 1.4-19.1), child being on an NVP-based regimen (versus EFV) (OR 3.2, 95%CI 1.3-7.7), fewer people helping give the child ART (OR 2.1, 95%CI 1.2-3.5), and the caregiver not being employed outside the household (OR 2.5, 95%CI 1.3-5.2).

Conclusion: Questioning the caregiver about their child's missed doses did not perform well as an adherence assessment strategy among this cohort of children. While certain factors may be associated with greater accuracy of caregiver reports, better adherence assessment strategies are urgently needed in this setting.

No conflict of interest

Abstract: P_24

Comprehensive Pediatric HIV care

Early infant diagnosis and linkage to care and treatment services at health facilities in Northern Ethiopia

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Introduction: In resource-limited settings, up to 40% of HIV-infected children not initiated on antiretroviral therapy (ART) will die by their first birthday. When ART is initiated within 12 weeks of life, infant mortality can be reduced by 75%.While Ethiopia is aiming towards realizing improved coverage in prevention of

mother to child transmission of HIV (PMTCT), timely testing and systematic monitoring and follow up of HIV exposed infants (HEI) remain a considerable challenge. According to the 2011 UNAIDS report, only 11% of the estimated 42,900 HIV exposed infants in the country received virologic testing in the first two months of age. Per standard of care in Ethiopia, infants determined to be HIV-exposed from PMTCT and other service entry points in the health facilities are referred to HEI clinics for HIV DNA polymerase chain reaction (PCR) testing and follow-up care. The objective of this study was to assess the practice of early infant diagnosis (EID) and evaluate linkages to care and treatment services for infants identified as HIV-infected in HIV exposed infant clinics in Northern Ethiopia.

Materials and Methods: We reviewed the HEI clinic registers from May, 2009, to June, 2011 in all public health facilities located in Bahirdar and Mekele cities in the Amhara and Tigray regions of Northern Ethiopia, respectively. Both cities were selected for the evaluation due to the high urban adult HIV prevalence (Bahrdar [11.9%] and Mekele [13.2%]). Structured data collection forms were used to collect relevant information from the HEI registers. Data were entered using Microsoft excel 2007 and analyzed using descriptive and Chi-square statistic.

Results: In Bahirdar, 461 infants were enrolled at the HEI clinics, with 303(66%) enrolled at ≤8 weeks of age, and 31 (6.7%) were HIV DNA PCR test positive at enrollment. Of 515 infants enrolled in HEI clinics in Mekele, 327 (63%) were enrolled at the age of ≤ 8 weeks, and 53 (10.3%) were HIV-infected. In Bahirdar, 0.3% (1/332)of infants referred from PMTCT were HIV-infected at entry to the HEI clinic compared to 23.3% (30/129)of infants referred from other entry points ($p<0.001$). In Mekele, 5.6% (20/354) of infants referred from PMTCT were HIV-infected at entry to the HEI clinic compared to 20.7% (33/161) of other infants ($p<0.001$). In Bahirdar 71% and Mekele 62%, of infants identified as HIV-infected were linked to care and treatment services.

Conclusions: In both Bahirdar and Mekele, more than a third of HIV exposed infants tested at the HEI clinics were older than 8 weeks. Infants referred from PMTCT programs were less likely to be HIV-infected at entry to the HEI clinic compared to infants referred from other entry points. While most HIV-infected infants are linked to treatment services, improvements are still needed. HIV programs should strive to improve uptake of PMTCT services. Programs also need to consider how to ensure enrollment of HEI's in care at the earliest recommended age and improve linkages to treatment services.

No conflict of interest

Abstract: P_25

Comprehensive Pediatric HIV care

Prevalence of paediatric HIV disclosure in a resource-limited setting

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Background: The paediatric HIV epidemic is concentrated in sub-Saharan Africa with nearly 90% of global paediatric HIV infections. Increasing antiretroviral therapy (ART) coverage has resulted in perinatally-infected children living to an age where it is essential they be told their HIV status as a fundamental aspect of their lifelong HIV care. In resource-limited settings the prevalence of HIV disclosure to children is generally low, despite the known positive outcomes of an age-appropriate, on-going disclosure process.

Methods: CHANGES (Childhood HAART Alterations in Normal Growth, Genes and aGing Evaluation Study) is a prospective observational follow-up study of perinatally HIV-infected children, aged 4-9 years, with the majority of children initiated on ART within the first 2 years of life. All children were initially enrolled onto clinical trials at 2 sites in South Africa namely ESRU (Rahima Moosa Mother and Child Hospital, Johannesburg) and PHRU

(Chris Hani Baragwanath Hospital, Soweto). At enrollment, caregivers are asked questions pertaining to disclosure, defined as an HIV-infected child being made specifically aware of their HIV status, and not only being told that they are ill. We describe the prevalence of disclosure across these two sites by age.

Results: 531 children were enrolled (ESRU=268; PHRU=263) of which 54.6% were female. Mean age at enrollment was 6.24 years (SD 1.5) and 7.14 years (SD 0.9) at ESRU and PHRU respectively. Overall only 8.6% had been disclosed to by enrollment: 5.3% at ESRU and 12.1% at PHRU.
Of the children aged 4-6 years, 3% had been disclosed to by the time of enrollment, 9.3% among the children aged 6-8 years and 17.4% of those aged 8-10 years. The age-specific rates of disclosure were significantly different between the sites: at ESRU 2.1%, 7.1% and 11.3% and at PHRU 7.4%, 10.1% and 27.3% had been disclosed to by enrollment at age 4-6 years, 6-8 years and 8-10 years respectively.
The mother/primary caregiver disclosed the HIV status alone in 38 (86.4%) of the cases, was assisted by others in 5 (11.4%), and disclosed to by the father in 1 case.
There were no significant differences in the caregiver demographics of the disclosed and undisclosed groups.

Conclusion: In keeping with previous studies, the prevalence of disclosure was low. Disclosure rates improved with age, but remain worryingly low in the age group approaching adolescence despite their involvement in HIV clinical trials for several years. Further studies are required to evaluate the barriers to and facilitators of discussing HIV with this vulnerable group and to develop effective supportive interventions.

No conflict of interest

Abstract: P_26

Implementation research on PMTCT and pediatric treatment programs

Assessment of a national early infant diagnosis program and linkage of HIV-infected infants to HIV treatment and care, Thailand 2008-2011

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Background: Linking HIV-infected infants to care and initiating antiretroviral therapy (ART) before 12 months of age reduces their risk of early death. The Thailand Early Infant Diagnosis (EID) Program provides 2 HIV DNA polymerase chain reaction (PCR) tests for HIV-exposed infants and ART for HIV-infected infants. We estimated the proportion of all HIV-infected infants in Thailand identified by the EID Program and successfully linked to care and ART.

Methods: The total number of HIV-exposed infants was estimated by multiplying the number of registered live births by the HIV prevalence among women giving births in hospitals. We estimated the total number of HIV-infected infants in Thailand by multiplying the estimated number infants born to HIV-infected mothers by nationally adjusted MTCT rates. The percentage of all HIV-infected infants identified by the EID program was defined as number of infants with at least one positive PCR test divided by the estimated

number of HIV-infected infants born. We assessed linkage to care and ART initiation by determining the proportion of infants with at least one positive PCR registered in the National AIDS Program database and initiated ART. The Chi square test was used to analyse annual linear trends.

Results: During 2008-2011, 13,761 of an estimated 22,573 (61%) HIV-exposed infants received EID. Of 22,573, an estimated 804 (3.6%) infants were HIV-infected, and 429/804 (53%) had at least one positive PCR test. Of the 429 PCR positive infants, 341 (79%) were linked to HIV care, 298 (69%) received a CD4 count result, 241 (56%) initiated ART, 157 (37%) initiated ART before one year of age, and 51 (12%) initiated ART before 6 months. The rate of ART initiation before 12 months of age increased from 28% in 2008, to 52% in 2011 ($p<0.01$).

Conclusions: The Thailand EID Program identified about half of all newly HIV-infected infants, and there is substantial 'leakage' in the cascade of identification to ART initiation. Active case management and increased coordination between PMTCT and pediatric care providers may improve the linkage to the care and ART initiation.

No conflict of interest

Abstract: P_27

Implementation research on PMTCT and pediatric treatment programs

Is Uganda reducing new pediatric HIV infections? Determining outcomes of HIV exposed infants at eighteen months

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Background: The nation of Uganda adopted the UNAIDS global plan of reducing new pediatric HIV infections by 90% by 2015 (UNAIDS Progress Report, 2012). Achieving this goal is dependent on a successful prevention of mother-to-child transmission (PMTCT) program capturing 100% of HIV pregnant mothers for initiation of treatment to protect the lives of mothers, provide HIV transmission prevention for their babies, while allowing for early infant diagnosis (EID) of those infants needing treatment (Ciaranello, Perez et al., 2012). Studies done in various sub-Saharan countries have shown that early treatment initiation for infants achieves low viral loads (Penazzato, Prendergast, Tierney, Cotton & Gibb, 2012). Uganda has implemented various initiatives such as tracking of HIV exposed infants and was the first country to implement Option B plus – lifelong treatment for all HIV pregnant mothers (Uganda EMTCT Fact Sheet, 2013). However, with all the measures the country has undertaken, the ministry of health acknowledges scarcity of data on outcomes of HIV exposed infants. The purpose of this project is to provide baseline data on outcomes of HIV exposed infants at eighteen months and the factors associated with them.

Methods: A retrospective analysis (N=1724) of abstracted data from 66 facilities representing 53 districts was conducted post entry into Epi-data using Strata 10 software. A total of 2039 data were collected and entered however, 315 were eliminated for exceeding the criteria of eighteen months. Descriptive statistics including frequencies and percentages was done to determine outcomes at eighteen months. Bi-varite analyses' using logistic regression was used to determine factors associated with loss, and Kaplan Meier function used to determine time to loss of infants testing negative at first DNA-PCR.

Results: At eighteen months majority of HIV exposed infants 70.2% were either lost to care or missing data; 22.9% tested negative and were discharged from care, 4.2% tested positive and were enrolled in care, while 1.8% died and 0.9% transferred to other facilities. Factors found to be associated with loss to care were an infant testing negative at first PCR, testing at age greater than 3months, the mother not being in PMTCT care, care giver not receiving results, and facility level.

Conclusion: Future efforts by Pediatric HIV programmatic work should focus on mentoring health workers on effective implementation of EID guidelines and documentation; quality improvement projects on EID processes in all facilities, including the evaluation of follow up measures of HIV exposed infants testing both negative and positive.

No conflict of interest

Abstract: P_28

Implementation research on PMTCT and pediatric treatment programs

Evaluation of 4 virological tests using DBS for HIV-1 early infant diagnosis: interpretation of discrepant results

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Background: An early diagnosis of the HIV-1 infection in infants born to infected mothers is critical for an early initiation of antiretroviral therapy and to reduce HIV-related mortality. Since HIV-1 antibodies from mother transferred across the placenta may persist in the child up to 18 months, it is required to detect HIV-1 genome (proviral DNA and/or viral RNA) or viral antigens for HIV-1 infant diagnosis. WHO recommends a second virological test on a separate specimen to confirm a positive result. We compared the sensitivity and specificity of four virological commercial assays (VCAs) for HIV-1 genome detection in dried blood specimens (DBS) from HIV-1-exposed infants.

Methods: Sixty eight infants born to HIV-1 infected mothers from Equatorial Guinea were selected. DBS were collected from November 2012 to December 2013 after spotting two drops of blood from each infant heel-prick onto each dot on a Whatman™ 903 Card by trained personnel and stored at -80ºC until use. Four VCAs were performed using one dot for each DBS following manufacturer's instructions, determining their sensitivity and specificity. Two were quantitative viraemia assays: Siemens VERSANT HIV-1 RNA 1.0 kPCR assay (kPCR) and Roche CAP/CTM Quantitative test v2.0 (Roche-VL-v2). The others tests were qualitative: CAP/CTM Qualitative Tests v1.0 (Roche-dx-v1) and v2.0 (Roche-dx-v2). The limit of HIV-1 detection in DBS ranged from 300 to 1,090 HIV-1 RNA copies/ml, detecting viral integrase (kPCR), Gag (Roche-dx-v1) or Gag+LTR (Roche-VL and Roche-dx-v2). Longitudinal DBS were collected in some infants to confirm positive molecular results and the seroreversion of antibodies to HIV-1 using at least 2 serological tests (ELISA, Abbott; Geenius™ HIV ½ Confirmatory Assay and Western Blot, BioRad).

Results: The mean age at first DBS collection was 2.4 months (range 1.2-4.9), 53% were female, 78% were born by vaginal delivery and 98.5% were not breastfed. Two HIV-1 infected infants (2.9%) were detected by the four VCAs in first and confirmatory DBS. HIV-1 was not detected in 49 (72%) children by any virological assay. We observed discrepant results between VCAs in the first DBS in 17 (25.1%) infants, detecting HIV-1 by some assays but not for others. HIV-1 infection was excluded in 12 of 17 cases using serological and virological testing in additional DBS collected when infants were from 5 to 14 months of age. We observed false positive HIV-1 diagnosis in 9 (13.2%), 8 (11.8%), 2 (3.6%) infants using dx-v1, VL-v2 and dx-v2 Roche assays, respectively, but none using kPCR. No false negative results were found by any technique. Thus, although the 4 assays presented 100% sensitivity, only kPCR showed 100% specificity, followed by Roche-dx-v2 (96.2%), Roche-VL-v2 (87.9%) and Roche-dx-v1 (86.4%).

Conclusions: VCAs using DBS were useful for early infant HIV-1 diagnosis in settings with low HIV-1 mother-to-child transmission rates. More efforts are required to increase specificity of VCAs. We found a significant proportion of false positive results that might result in wrong

diagnosis and unneeded treatment. We propose the use of a second different virological assay in DBS when first result is positive, especially for those with lower viral loads.

No conflict of interest

Abstract: P_29

Implementation research on PMTCT and pediatric treatment programs

The pediatric antiretroviral therapy (ART) cascade: ART eligibility, initiation and retention among children under 5 years in Tanzania.

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Introduction: WHO recently recommended antiretroviral therapy (ART) for all children < 5 years(y). As countries consider this guidance, we analyzed recent (2010-2012) pediatric ART eligibility assessment, ART initiation and retention among children < 5y in Tanzania.

Methods: Children initiated ART according to 2008 WHO recommendations. Retrospective cohort analyses of routinely collected data at ICAP-Columbia University-supported clinics were conducted under Optimal Models. Children were categorized as infants: 0-11 months(m), and children 12-59m: including younger children(YC) 12-35m and older children(OC) 36-59m. We examined ART eligibility (CD4+ count/WHO stage) assessment and estimated correlates of being ART eligible at enrolment using logistic regression models. Among those ART eligible, patient and facility factors were evaluated for independent association with ART initiation at study clinic in survival analyses taking death and lost-to-follow-up as competing risks.

Results: 1679 children enrolled at 69 clinics: 469(28%) infants, 780(46%) YC, and 430(26%) OC. All but 9(0.5%) had ART eligibility assessment: 99% had WHO staging and 25% CD4+ counts. Overall, 62% were ART eligible at enrolment: 100% infants, 51% YC, 40% OC. Children more likely to be ART eligible were: YC (vs OC) Adjusted sub-distribution Hazard Ratio, AsHR (95% Confidence Interval): 1.6(1.2-2.0); enrolled as inpatients (vs VCT): AsHR 2.1 (1.5-3.0); and at urban clinics (vs rural): AsHR 2.2(1.4-3.6). ART initiation among infants was 46%, 53% and 62% at 3, 6, and 12m; among children, 47%, 57% and 62% . Infants were more likely to initiate ART if enrolled in 2012 (vs 2010): AsHR 1.8(1.2-2.5); and from PMTCT clinics (vs VCT): AsHR 2.0(1.3-3.0). Children were more likely to initiate ART if enrolled in 2011: AsHR 1.3(1.0-1.7) or 2012: AsHR 2.0(1.4-2.8); and less likely if missing enrollment CD4+ count 0.7(0.5-0.9), or attending secondary or private facilities (vs primary): AsHR 0.5(0.3-0.9) and 0.7(0.4-1.0) respectively. Of eligible children who started ART, 66% infants and 77% children were on ART 12m later.

Conclusions: Nearly all children were assessed for ART eligibility, but ART initiation was sub-optimal and infants did not universally initiate ART. Better pediatric ART initiation in 2012 and from PMTCT clinics may reflect recent efforts towards integration and improving linkages between PMTCT, early infant diagnosis and ART services.

No conflict of interest

Abstract: P_30

HIV infection and adolescents

Final height and associated factors in perinatally HIV-infected Asian adolescents

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Introduction: Low height has been associated with lower quality of life and self-esteem for adolescents. There are limited data on final height (FH) of HIV-infected youth in Asia.

Methods: We analysed data of perinatally HIV-infected adolescents age ≥18 years at their last clinic visit in 18 clinics in six countries in the TREAT Asia Pediatric HIV Observational Database. They were initiated on combination antiretroviral therapy (cART) after January 2003. FH was defined as height at age 18 years old. Height-for-age z-score (HAZ) was calculated by using the 2007 WHO Growth Reference. Stunting was defined as HAZ <-2.0. Logistic regression analysis was used to identify predictors of FH.

Results: There were 273 children with reported height measurements at age 18; 60% were female. The majority (92%) were from Thailand, 4% from Cambodia, and the remaining 4% from India, Vietnam, and Malaysia. At cART initiation, median (IQR) age was 11.4 (10.2-12.7) years, 53% had WHO stage III/IV, median CD4% was 5%(2-11%), median CD4 was 161(23-226)cells/mm^3, and HIV-RNA was 5.0 (4.6-5.4) $\log_{10}$ copies/ml. For those with available measurements at cART initiation (N=194), median HAZ was -2.2 (-3.2 to -1.4), 106 (55%) were stunted.
At age 18, median (IQR) HAZ was -1.6 (-2.5 to -1.0) for boys and -1.4 (-2.1 to -0.9) for girls. Overall, median FH was 164 (157-169) cm for boys and 154 (149-157) cm for girls. Eighty three (30%) of children were stunted; 38/110 (35%) of boys and 45/163 (28%) of girls. Among those who were stunted at age 18, median FH was 156 (153-158) cm for boys and 147 (144-149) cm for girls.
Among those stunted at cART initiation, 51 (48%) remained stunted at age 18 years. In the multivariate analysis, those with baseline HAZ <-1.0 ($p<0.001$) and girls ($p<0.0001$) had shorter FH.

Conclusion: Overall, one-third of perinatally HIV-infected adolescents in this regional cohort were stunted at age 18 years. Approximately half of those who were stunted at cART initiation remained stunted over time.

No conflict of interest

Abstract: P_31

HIV infection and adolescents

Transition Needs of Children and Youth Living with HIV in Vietnam

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Introduction: Pediatric antiretroviral therapy (ART) was introduced in Vietnam in 2005, and children and youth living with HIV (CYLH) are now increasingly surviving into adolescence. CDC/PEPFAR supports pediatric HIV treatment sites in 20 provinces, representing ~40% of CYLH nationwide. Pediatric care focuses on ART provision and opportunistic infection treatment, with limited time or capacity for transition preparation. National regulation requires that CYLH transfer to adult clinics after age 15. We assessed the transition needs of CYLH and staff at CDC/PEPFAR-supported sites.

Methods: A cross-sectional review of CYLH enrolled at 21 sites was conducted, including collection of demographic and clinical data. Health care workers (HCWs) at each site were surveyed regarding staff preparedness and concerns about transition.

Results: Of 1,660 CYLH, 27% were aged >10 and 42% were orphaned (lost one or both parents). Among CYLH >10, 33% were fully disclosed, 10% had adherence <95% and 15% were on secondline ART. Sites had transitioned 30 patients in the previous 3 years; 3% refused transfer and returned to pediatric clinic, and 7% were lost to follow-up (LTFU). Six sites continued providing care for patients >15. Only 5 sites had social workers and/or psychologists on staff. 26% of HCWs had received training on pediatric HIV disclosure, 7% on adolescent sexuality/reproductive health, and 3% on transition. Common concerns regarding adolescents related to lack of social support (81%), sexual/reproductive health education (43%), adherence and LTFU (33%), and disclosure (14%).

Conclusions: More than 1/4 of CYLH in Vietnam will transition to adult care in the next 5 years, but only 1/3 of these know their HIV status and many have risk factors for poor outcomes. A locally adapted adolescent transition program and national guidance for HCWs are being developed to support CYLH to acquire necessary knowledge and skills for self-care, adherence, safer sex, and reproductive health.

No conflict of interest

Abstract: P_32

HIV infection and adolescents

Gag-specific CD8 T-cell proliferation in youths with perinatally acquired HIV-1 infection: The ANRS-EP38-IMMIP Study

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Introduction: The ANRS-EP38-IMMIP study aimed to provide a detailed assessment of the immune status of perinatally infected youths living in France. We present here our findings for the proliferation of Gag-specific CD4 and CD8 T cells, constituting major immune correlates of viral control, and the association between the proliferation of these cells, HIV disease history and immune markers.

Methods: The ANRS-EP38-IMMIP study included 93 perinatally HIV-infected youths aged between 15 and 24 years. Fifty-three were on ART and aviremic at the time of the study, had undergone valid T-cell proliferation assays and were included in the final analysis. Twenty-four of these 53 patients (45%) were male, and 19 (36%) were black. Gag-specific T-cell proliferation was quantified on fresh PBMCs, with a CFSE-based flow cytometry assay. Plasma analytes were quantified by ELISA or multiplex assays. Peripheral blood cells were phenotyped by flow cytometry.

Results: Gag-specific proliferation of CD4 and CD8 T cells was detected in 11 (21%) and 22 (42%) patients, respectively. The proliferation of Gag-specific CD4 and CD8 T cells was more frequent in black patients than in patients from other ethnic groups (CD4: 47 vs. 6%, *P*=0.0009; CD8: 68 vs. 27%, *P*=0.008). The CD8 responders (CD8R) had a shorter duration of viral suppression than CD8

nonresponders (CD8NR) (54 vs. 20 months, *P*=0.04). In multivariate analyses, including sex and HIV-1 subtype as covariables, Gag-specific CD4 T-cell proliferation was associated with ethnicity only, whereas Gag-specific CD8 T-cell proliferation was associated with both ethnicity and duration of viral suppression. Both CD4 and CD8 responder patients reached their nadir CD4 T-cell percentages at a younger age than their nonresponder counterparts (6 vs. 8 years, *P*=0.04 for both CD4 and CD8 proliferation). However, these associations were not significant in multivariate analysis.
Further studies of the associations between Gag-specific T-cell proliferation and the immune environment showed higher levels of plasmacytoid dendritic cells in CD4R patients than in CD4NR patients (13 vs. 7 cells/µl, *P*=0.001). This association remained significant after adjustment for ethnicity. CD8R patients tended to have higher $CD127^{low}CD25^{high}$ regulatory T cell (Treg) percentages (5.6 vs. 5.0%, *P*=0.07), and a lower proportion of naive $CD45RA^{+}CCR7^{+}$ cells among Tregs than CCD8NR patients (49 vs. 58%, *P*=0.07). The percentages of CD4 and CD8 T lymphocytes expressing the gut-homing α4β7 integrin were higher in CD8R than in CD8NR patients (CD4: 6 vs.10%, *P*=0.007; CD8: 9 vs.18%, *P*=0.007). After adjustment for ethnicity and duration of viral suppression, plasma TGF-beta1 concentration, naive CD4 Treg and $\alpha4^{+}\beta7^{+}$ CD8 T-cell levels were found to be significantly associated with Gag-specific CD8 T-cell proliferation.

Conclusion: After at least 15 years of HIV infection, black adolescents and young adults were found to display more frequent Gag-specific T-cell proliferation than patients of other ethnic groups, despite being born in the same country, with similar access to care. The main immune correlates of preserved Gag-specific T-cell proliferation were the levels of dendritic cells, the anti-inflammatory cytokine TGF-beta1, Treg differentiation, and T cells with a gut-homing phenotype.

No conflict of interest

Abstract: P_33

HIV infection and adolescents

Kenyan Caregivers' Perspectives and Preferences for Disclosing HIV Status to Infected Children

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Introduction: As HIV-infected children survive into adolescence and adulthood at unprecedented rates, care programs in resource-limited settings must support child HIV disclosure. We explored caregiver views on HIV disclosure to children enrolled in a large care system in Kenya.

Methods: We conducted a qualitative study using focus group discussions (FGDs) with 61 caregivers of HIV-infected children receiving HIV care at three clinics in western Kenya. Separate FGDs were held for caregivers who had done child HIV disclosure and those who had not. A trained facilitator led the FGDs in Kiswahili (a widely used regional language) using a semi-structured interview guide based in grounded theory and covering multiple aspects of beliefs about HIV and disclosure. FGD recordings were translated into English, transcribed, and analyzed using constant comparison, progressive coding and triangulation to arrive at a contextualized understanding of caregivers' HIV disclosure preferences.

Results: Sixty-one caregivers of HIV-infected children, the majority of whom were mothers of HIV-infected children, participated in 8 FGDs. Caregivers strongly endorsed a process of gradual HIV disclosure, which was considered psychologically easier for the child and allowed time for children to internalize and process information. Caregivers stressed that disclosure should be done by someone close to the child who is sensitive to the child's emotional state and can offer hope. A child's readiness for disclosure was informed by a

child's age (preferring 10-15 years), maturity, children asking questions, and demonstrations of medication non-adherence or worsening disease course. Caregivers balanced the perceived risks of telling a child who is too young with the risks of waiting too long. Although caregivers wanted to be the ones to disclose and decide disclosure timing, they wanted clinician assistance in educating the child and themselves, asking and answering questions, and being present during disclosure. Caregivers identified counseling services, peer group support, and cultural- and age-appropriate disclosure-related materials or technology as valuable.

Conclusions: Kenyan caregivers endorsed a gradual HIV disclosure process to older children in which they were the primary decision-makers, with strong support from the health care team. Better understanding caregivers' preferences may improve the design and implementation of disclosure support and interventions.

No conflict of interest

Abstract: P_34

HIV infection and adolescents

What promotes successful transitioning of adolescents living with HIV from pediatric to adult care settings?

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Background: Although the perinatally HIV-infected population in Asia is now aging into adulthood, little is known about factors influencing successful transitioning of adolescents from pediatric to adult care.

Methods: Questionnaires and in-depth interviews were conducted with a convenience sample of adolescents who had been transferred to adult HIV care for ≥6 months at three tertiary referral hospitals in Thailand and Vietnam. Informants were asked about their experiences before, during and after transitioning.

Results: The 14 informants (71% female; 21% Vietnamese) were recruited between June - July 2013. Median age was 20 years. At the time of the study, median time in adult care was 24 months, 64% were double and 29% were single orphans; 58% reported being in committed relationships; 85% were employed doing either full-time or part-time work. All were taking antiretroviral therapy (ART); 6 of 9 who knew their viral load results had undetectable virus at their last clinic visit. Counseling about the need to transition occurred at a median age of 17.2 years, and transfer to the adult clinic at a median age of 19.8 years. Almost all (93%) felt the pediatric care teams were actively involved in the transition preparation process, compared to 50% for the adult care teams. Reasons reported for transition included age restrictions at the pediatric clinic, policies of the national treatment program, limitation of pediatric clinic space, and moving to a clinic closer to home. Although 86% felt they had been adequately prepared for transitioning by healthcare providers and acknowledged responsibility for their disease management, 58% did not feel comfortable receiving care at adult clinics and 28% admitted their ART adherence had worsened after transitioning. Loss of supportive relationships with their pediatric healthcare team and questions about the quality of care in the adult clinic were prime concerns before transitioning. Post-transition, respondents reported early difficulties in physically navigating the adult HIV care system (e.g., clinic to pharmacy to lab). Fear of having their HIV status disclosed to people they might know through the adult clinics caused anxiety for some informants. Interventions that helped adolescents better prepare for the transition included workshops to build confidence and guided tours of the adult HIV clinics with introductions to key clinic staff. Recommendations from adolescents to improve the transition experience included shared decision-making on when to transition,

having pre-transition orientations and introductions to the adult care teams, and having specialized clinics for young adults.

Conclusions: In this exploratory study, adolescents who went through a structured transition process felt more confident, but remained uncomfortable during the early part of their care in adult HIV clinics. These findings emphasize the need for pediatric and adult clinics in Asia to work together to better prepare for the transition of patients who have had to cope with the social and developmental impact of life-long HIV. Optimizing HIV transition models will require greater input from adolescents before and after taking these steps.

No conflict of interest

Abstract: P_35

HIV infection and adolescents

Young And Resilient: HIV-Infected Adolescents After Transition To Adult Care

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Introduction: Little is known on outcomes after transition and in early adulthood among the first wave of survivors of perinatal HIV infection. The objective of this study was to assess clinical outcomes and quality of life measures after transfer to adult care.

Material & Methods: Clinic records were reviewed to identify all youth who transitioned from the Centre Maternel et Infantile sur le Sida pediatric HIV clinic (Montreal) at age 18 to an adult care provider between 1999-2012. Inclusion criteria for the study included 1) perinatal HIV infection 2) engaged in care prior to transfer (attendance at least 3 appointments per year in the two years prior to transfer) 3) capacity to communicate (verbally or written) 4) minimum elapsed time of at least 1 year since transfer. Patients were contacted for consent to enter into the study using last available patient or parental listed phone number on hospital record, internet based telephone directory or social media (facebook). A standardized questionnaire was administered by telephone or in-person interview, and copies of current medical records obtained from treating physicians.

Results: 45 patients were transferred between 1999-2012, among whom 25 consented to the study, 8 were lost to follow-up, 8 refused participation, and 4 were deceased. Mean time since transfer was 3.83 years (range 1.11 - 6.78). Overall, 83% of patients remained engaged in care, defined by at least one physician visit within 6 months of the interview. Sixty-four percent of interviewees were still in a school setting, and 33% had completed their training to date. Highest degree obtained at time of interview was no high school (40%), high school (36%), professional degree without highschool (16%) and college (8%). Eighty percent of the youth stated that they had regular sexual partners, to whom only half routinely disclosed their HIV status. Twenty-five percent reported ever having been diagnosed with an STI Among women, 46.7% reported using the morning after pill as emergency contraception for an average 2.42 times (range 1-4), 40% had had a first pregnancy, and overall, 22% of the youth had become parents themselves. 65.2% of patients reported difficulty with drug adherence to their current regimens, with 17.4% not taking any medication. A third of patients did not know their current CD4 count or viral load. At one-year post-transfer, there was a statistically significant decrease in absolute CD4 count (mean 370 vs 524 cells/mm3, p=0.04), however, there were no significant changes in viral load (mean 2.42 vs 2.55 $\log_{10}$ copies/mL, p=0.47). Overall, 95% reported they would have preferred to stay in pediatric care for longer.

Conclusions: This group of youth remained engaged in care without significant change to their medical status post-transition, though selection bias was likely present among those who were successfully recruited. Nonetheless,

difficulties with drug adherence, disclosure to partners, and lack of disease-related knowledge were identified as issues in their post-transition care.

No conflict of interest

Abstract: P_36

HIV infection and adolescents

Low level of HIV diagnosis disclosure to HIV-infected children age 7 to 12 years old, Kampala, Uganda

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Background: At the end of 2013, there were an estimated 3.1 million children < 15 years living with HIV, with almost 90% residing in sub Saharan Africa. With increased availability of antiretroviral therapy (ART) and improved care, increasing numbers of perinatally infected children are surviving into adolescence. As paediatric HIV care and treatment programs are expanding, a growing challenge facing health providers and caretakers is disclosure of HIV serostatus to infected children. This study aims to determine the prevalence and determinants of HIV disclosure to HIV-infected children age 7 to 12 years old in an urban setting in Uganda, and to explore caretaker (i.e.,parents/primary guardians) perceived barriers to and experiences with disclosure.

Methods: Between August and October 2013, caretakers of HIV-infected children age 7 to 12 years old enrolled in care at a large pediatric HIV clinic in Kampala, Uganda were consecutively recruited to participate in a semi-structured interview to assess prevalence of pediatric HIV status disclosure, reasons for disclosure or nondisclosure, and caretaker reported experiences of their own and their child's experiences following disclosure. Disclosure was the primary outcome, dichotomized as full disclosure and no or partial disclosure. We assessed whether child age and ART use was predictive of full disclosure, adjusting for caretaker age, education, and employment.

Results: 66 of 77 eligible caretakers (94% mothers, 6% fathers) were enrolled, all of whom were also HIV-infected.The majority (98.5%) had disclosed their own HIV-positive status to at least one member of their household. Although the majority (87%) of children were taking ART medications, only 22 (31.9%) were reported by caretakers to have been disclosed to fully. The odds of disclosure increased with child's age (AOR 2.67, 95% CI 1.58 to 4.51). Child ART use was not predictive of disclosure (AOR 0.9, 95% CI 0.14 to 5.61).

Conclusions: Disclosure of HIV diagnosis to children by age 12, as recommended by the World Health Organization, remains very low despite evidence of positive effects for children who are told their HIV-positive status prior to transitioning to adolescence. Culturally and developmentally appropriate interventions that respond to the needs of caretakers and children in the specific context of HIV disclosure are needed.

No conflict of interest

Abstract: P_37

HIV infection and adolescents

Adolescent HIV Implementation Tools - focusing on transition

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Introduction: Adolescence is a time of vibrancy, exploration and self-discovery. Many

adolescents take risks to fit in with peers and develop more autonomy, resulting in increased vulnerability to HIV. Female adolescents in sub-Saharan Africa face a higher risk of infection than their male peers. Adolescent members of key populations are also at higher risk for HIV acquisition or transmission through sexual transmission and injecting drug use. Additionally, recent data from sub-Saharan Africa indicates many children infected perinatally are entering adolescence, with 36% having a median survival age of 16, even without access to ART creating an un-planned for population coming of age in the pediatric system. The transition into adulthood consists of major psychological, biological, and social changes resulting in unique healthcare needs, further complicated by HIV which is marked by high loss-to-follow-up and lower adherence rates among adolescents.

Description: To provide implementation guidance for healthcare providers working with adolescents living with HIV (ALHIV), the World Health Organization has developed an interactive tool that is used as a companion guide for the 2013 WHO guidance- *HIV and Adolescents: Guidance for Testing and Counselling and Care for Adolescents Living with HIV*. The tool illustrates and amplifies the recommendations of the formal guidelines with practical guidance and multi-format resources for providing effective adolescent-friendly HIV testing and counselling, treatment and care services. The tool also covers operational considerations for effective implementation of the recommendations. The interactive tool integrates tools from a number of resources including the *Toolkit for Transition of Care and Other Services for Adolescents Living with HIV*. The Toolkit provides guidance for care providers transitioning ALHIV from pediatric to adult-focused services. To increase self-management of care, the Toolkit provides important tools and information on psychosocial development, mental health, sexual and reproductive health, protection, alcohol and substance use, beneficial disclosure, loss grief and bereavement, clinical considerations and positive living for providers, family/caregivers and ALHIV.

Proposal: We would like to present the interactive tool to inform health and community care providers on the tools available to assist them in carrying out the new WHO guidance. The Toolkit will also be presented to increase understanding of the transition process and how it may be used to increase self-management of HIV care in a holistic and methodical manner.

Objectives:

- Acquaint care providers with WHO Guidance on HIV Counseling, Testing and Care for ALHIV;
- Demonstrate use of the interactive tool and its utility in enacting WHO guidance;
- Describe transition issues and processes for ALHIV;
- Share the Toolkit and its utility to promote a smooth transition.

Conclusion: Participants will depart the workshop with knowledge of the various tools that are available as they provide holistic testing, care, and treatment services for ALHIV.

No conflict of interest

Abstract: P_38

HIV infection and adolescents

Pediatric and adult HIV care providers agree on the importance of developmental readiness in the transition of youth living with HIV from pediatric to adult care

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Introduction: Transition of youth living with HIV/AIDS (YLHA) from pediatric to adult care can be challenging. We conducted a national survey of Canadian HIV care providers (HCPs) to assess transition practices and perceptions, focusing on developmental readiness and perceived outcomes.

Material & Methods: A 32-item questionnaire was developed to assess current practices and perceptions of HCPs with respect to transition of YLHA to adult care. The questionnaire was distributed on-line to pediatric and adult HCPs,

including physicians, nurses, and allied health professionals, across Canada.

Results: Ninety-six HCPs responded to the survey, including 59 (61%) adult and 37 (39%) pediatric providers. Half (51%) of respondents were physicians, and most (70%) had participated in less than 10 patients' transition to adult care. The majority of respondents' programs transitioned YLHA at 18 years (64% adult, 56% pediatric), with another quarter to fifth (20% adult, 25% pediatric) transitioning between ages 18-25 years based on developmental readiness. Although the majority of YLHA in Canada are transitioned at age 18, most adult and pediatric HCPs did not believe that all YLHA should be transitioned at that age (64% and 75%, respectively). Most adult and pediatric HCPs agreed that 'developmental readiness' is a barrier to successful transition; 84% and 94% identified this as a 'large' or 'moderate' barrier, as opposed to 'small' or 'not.' One third of respondents reported 'poor' or 'fair' medical outcomes (34% adult, 35% pediatric) post-transition versus 'good' (47%, 50%) or 'very good' or 'excellent' (19%, 15%). 'Poor' or 'fair' engagement and retention in care outcomes post-transition were reported by 42% of adult and 51% of pediatric HCP respondents.

Conclusions: Most YLHA in Canada are transitioned to adult care at age 18, largely due to institutional requirements. Clearly, there is a discrepancy between this practice and both adult and pediatric HCPs' beliefs. A minority of HCPs – whether adult or pediatric – believe their patients' outcomes to be 'very good' or 'excellent' after transition. YLHA in Canada may benefit from specialized programs for 'young adults' (13-24 years), designed specifically to address developmental readiness and achieve successful transition.

No conflict of interest

Abstract: P_40

Prevention of Mother-to-Child transmission

Retention in care among HIV-infected women initiating ART during pregnancy: a cohort study

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Background: Recent international guidelines call for universal use of triple-drug antiretroviral therapy (ART) in HIV-infected women during pregnancy and postpartum. There are however concerns regarding potentially high levels of non-adherence and/or disengagement from care that may attenuate the benefits of ART for HIV transmission and maternal health. We investigated missed visits and disengagement among women initiating ART during pregnancy in Cape Town, South Africa.

Methods: A cohort study was conducted of women starting ART, Jan 2011-Sept 2012, at a large primary care antenatal clinic (ANC). Eligible women were identified in PMTCT services based on CD4 ≤350 cells/µL, and women initiated a regimen of tenofovir, lamivudine and efavirenz. Outcomes were measured up to 6 months postpartum: (i) disengagement (>56 days late for a scheduled visit) and (ii) missed visit (returning to care 14-56 days late for a scheduled visit).

Results: A total of 358 women (median age, 28 years; median gestational age at initiation, 26 weeks) initiated ART during pregnancy. By 6 months postpartum 24% of women (n=86) had missed at least one visit and 32% (n=115) had disengaged from care. Overall, 49% of women had either missed a visit or disengaged by 6 months postpartum. Disengagement was more than twice as frequent postpartum

compared to in the antenatal period (6.2 vs 2.4 per 100 woman-months, respectively; p=0.0004). In a proportional hazards model, later gestational age at initiation (HR: 1.04; 95% CI: 1.00-1.07; p=0.030) and being newly diagnosed with HIV (HR: 0.63; 95% CI: 0.43-0.94; p=0.022) were significant predictors of disengagement from care after adjusting for patient age, starting CD4 cell count and site of ART initiation.

Conclusions: These results demonstrate that HIV-infected women initiating ART during pregnancy frequently disengage from care, particularly post-delivery. Further research is required to understand reasons for non-adherence and disengagement from care and the implications thereof in the context of pregnancy. Women newly diagnosed with HIV and those presenting for ANC at later gestational ages may be particularly vulnerable and there is an urgent need for interventions to promote retention among all HIV-infected women during pregnancy and after delivery.

No conflict of interest

Abstract: P_41

Prevention of Mother-to-Child transmission

Prevalence and Predictors of Low Vitamin D Status in HIV-infected Pregnant Women in Central and South America

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Background: Vitamin D deficiency and insufficiency are common in pregnancy worldwide. Studies of vitamin D levels in pregnancy are scarce in Latin America. Few studies have evaluated vitamin D status in HIV+ pregnant women.

Materials and Methods: We evaluated data from HIV+ pregnant women in Latin America (Argentina, Bahamas, Brazil, Jamaica, Mexico, & Peru) enrolled in the National Institute of Child Health and Human Development (NICHD) International Site Development Initiative (NISDI) prospective cohort study from 2002-2009. Using repository blood specimens collected at 12-34 weeks' gestational age (GA), we measured plasma maternal 25-hydroxyvitamin D [25(OH)D], the precursor active vitamin D, levels by the Abbott Architect® immunoassay. Vitamin D deficiency was defined as 25(OH)D <20 ng/mL, insufficiency as 21–29 ng/mL, and sufficiency as >30 ng/mL. Prevalence estimates including 95% confidence intervals (95%CIs) were calculated using the exact binomial method. Logistic regression modeling was used to identify factors associated with low vitamin D status defined as levels <30 ng/mL (deficiency and insufficiency combined).

Results: After excluding women enrolled after 35 weeks GA (177), those without antenatal blood specimens (60), and repeat pregnancies (47), 715 HIV+ pregnant women were included in analysis. Mean age and GA was 28.6 years [standard deviation (SD)=5.7] and 25 weeks (SD=6.3) respectively at the antenatal visit. Five hundred forty-two (76%) completed ≥7 years of education, 189 (26%) were gainfully employed, 417 (58%) resided in subtropical latitudes, 136 (19%) had their vitamin D sample collected during winter, and 159 (22%) reported tobacco use during pregnancy. Marijuana was the most frequent illicit substance used during pregnancy (4%). One hundred twelve (16%) had a CD4+ count <200 cells/mm³, 322 (45%) had an HIV RNA level ≥1000 copies/mL, and 70 (10%) were CDC HIV class C at enrollment. Three hundred twenty-two (45%) received ≥ 28 days of 3-drug combination antiretroviral therapy (cART) at the time of the vitamin D assessment. At the antenatal visit, 30.5% (95%CI: 27.1-33.9) were vitamin D deficient, while 35.2% (95%CI: 31.7-38.7) were insufficient, and 34.3% (95%CI: 30.8-37.7) were sufficient. In multivariate analysis, factors associated with increased risk of low vitamin D status [odds ratio (OR), 95%CI] included: residence in subtropical

latitudes (OR=1.97, 1.35-2.88); vitamin D assessment during a non-summer season [autumn (OR=1.85, 1.20-2.86), spring (OR=4.3, 2.65-6.95), winter (OR=10.82, 5.74-20.41)]; vitamin D assessment at < 20 weeks GA (OR=1.89, 1.18-3.03); and being employed (OR=1.59, 1.06-2.38). Factors associated with decreased risk of low vitamin D status included lower CD4+ count <200 cells/mm³ (OR=0.45, 0.26-0.77) and 200-499 cells/mm³ (OR=0.60, 0.40-0.89)], and receipt of a PI-based regimen (OR=0.62, 0.40-0.95).

Conclusions: The prevalence of low vitamin D status was high (>60%) amongst HIV+ pregnant women in Latin America despite residing in tropical/subtropical latitudes. Those in subtropical latitudes and earlier GA seem to be at higher risk, and those assessed after summer had an increased risk through autumn, winter and spring. Receipt of PI-based cART appears to be protective. Further studies to identify those with poor vitamin D status may impact monitoring, choice of cART in pregnancy, as well as timing of nutritional interventions.

No conflict of interest

Abstract: P_42

Prevention of Mother-to-Child transmission

In utero antiretroviral exposure, birth weight and growth of HIV-exposed uninfected children in Brazil

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Context: Option B+ consists of universal lifelong antiretroviral therapy (ART) for all pregnant and breastfeeding women. Consequently more fetuses will be exposed to ART. There are concerns about the effects of in utero exposure to ART on the development of HIV exposed but uninfected (HEU) children.

Objectives: To evaluate whether in utero exposure to ARVs is associated with lower birth weight/height and reduced growth during the first two years of life.

Design: Cohort study of HEU babies followed up for two years after birth.

Setting: Tertiary children's hospital in Rio de Janeiro, Brazil, that cares for over 1,000 HEU infants.

Study population: HEU babies (defined as babies born to HIV infected mothers: at least one serological test positive; and the babies had at least one HIV-viral load<400 copies/mL in their first six weeks of life) born between 1996-2010 with at least one follow up visit. Multiple pregnancies andchildren with congenital abnormalities were excluded.

Main outcome measures: Weight was measured by mechanical scale, and height was measured by a measuring board. Z-scores for weight-for-age (WAZ) and length-for-age (LAZ) were calculated using the 2006 WHO child growth standards. We modeled trajectories by mixed-effects models and adjusted for mother's age, CD4 cell count, viral load, year of birth and family income.

Results: A total of 588 HEU infants were included, 275 (47%) were female, and the median gestational age at birth was 38 weeks. Among all infants, 155 (26%) were not exposed in utero to ART, 114 (19%) were exposed in the first trimester and 319 (54%) were exposed later in second and third trimester. WAZ scores were lower among infants exposed early compared to the other children: adjusted difference -0.52 (95% CI -0.99 to -0.04) at birth and -0.22 (95% CI -0.47 to 0.04) during the two-year follow-up. Although LAZ scores at birth were similar between infants exposed early or later (-0.05 (95%CI=-0.41 to 0.30)), the LAZ scores were lower during follow-up if exposed early: -0.35 (95% CI -0.63 to -0.08). Z-scores of infants exposed later during pregnancy were similar to ARV unexposed infants.

Conclusions: In HEU children, early in utero exposure to ARVs was associated with reduced growth up to 2 years of life, even after adjusting for baseline maternal health and socioeconomic characteristics. In the context of option B+, the growth of HEU children needs to be monitored closely, considering in utero ARV exposure.

No conflict of interest

Abstract: P_43

Prevention of Mother-to-Child transmission

Developing an efficient early infant diagnosis program to ensure universal access in Swaziland

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Background: The Swaziland National ART Program was started in 2004 and by 2013 pediatric ART coverage reached 70% of the projected ART recipients <15 years. From 2007 early HIV infant diagnosis (EID) became available using DNA-PCR testing for children <18 month. It continuously improved efficiency, increased access and reduced turnaround time for results in the following years. The EID program represents a success story for Swaziland's pediatric HIV response and has been a key intervention to increase the number of pediatric ART recipients. In this analysis we review the most important milestones and game changers that increased to HIV testing for this very important population at risk of HIV infection.

Material and Methods: We reviewed routine retrospective program data for the EID program in children <18 months from inception in 2007 until 2013. Data was extracted from routine quarterly national level dashboards of DNA-PCR testing, absolute numbers and trends were analyzed. Also, we tracked historic records about sample transportation, specimen logistics, laboratory processes and results delivery.

Results: The EID program provides sample collection and transports results to over 150 facilities; sample processing in the government system is conducted at a central laboratory (NRL). The number of first DNA-PCR tests (infants <18 months) increased from 2,570 in 2007 to 11,596 in 2013 (20% and 86% coverage of HIV-exposed infants). The number of HIV positive tests was 477 (18.5%) in 2007 and 535 (4.6%) in 2013. Sample rejection rate is consistently less than 1%. Turnaround time for results decreased by 50% from 4-6 weeks in 2007/2008 to 2-3 weeks in 2013. Ensuring sample processing is done within the NRL in Swaziland provided for this reduction in turnaround time: currently sample processing takes less than two days at the NRL. In 2010, a 'DBS hotline' was introduced allowing health care workers (HCWs) to call for DBS results; in 2012 the system was expanded to proactively alert HCWs about positive PCR results to spur action by tracing the infant in the community. In 2013, averages of 140 calls were received and 40 calls made for positive results every month.

Conclusions: The ability to cope with growing sample volumes and consistently deliver results-with a focus on HIV positive results- is the key success of the Swaziland EID program. Intense capacity building, quality assurance, support to the sample transportation system and innovative thinking are fundamental to guarantee timely availability of results to the end users. The Swaziland EID program provides a robust system for universal access and more efficient delivery of results. Support to HIV care in infants need to include laboratory and clinical collaboration. There is a need to evaluate to what extend these efforts influence early access to ART in infants.

No conflict of interest

Abstract: P_44

Prevention of Mother-to-Child transmission

Using internet-based tools to facilitate communication in a multi-country PMTCT collaborative

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The Partnership for HIV-Free Survival (PHFS) has explored the effectiveness of using several internet-based tools to facilitate the spread of knowledge within a collaborative model from front-line health care sites to other collaborative countries. This spread is one vehicle driving PHFS' overall goal: to reduce MTCT by 90% in member countries Kenya, Uganda, Tanzania, Mozambique, South Africa, and Lesotho.

PHFS' collaborative model includes a steering mechanism led by each country's Department/Ministry of Health, alongside prototype sub-districts to test new ideas and tools, an all-country learning platform, and additional technical support provided by NGO partners. To harvest and share learning between countries, PHFS utilizes several internet-based tools when in-person meetings are not feasible. The tools that PHFS has explored to date are cross-country webinars, email groups, social media (Twitter and Facebook), and email newsletters. All country teams are encouraged to share PMTCT-related results, challenges, and successes. IHI has identified data related to the use of these tools by exploring, where available: (1) the number of times each tool has been used since the start of PHFS, (2) the number of times partner organizations and country teams have used each tool, and (3) the type of content communicated through each tool (in the categories of external resources or data; PHFS-specific resources; data and questions; general updates on country progress; and other content).

In total, PHFS has held 5 cross-country webinar calls. On these calls, all 10 partner organizations, and all six (100%) country teams have shared information. On two occasions (40%), one country team has shared PHFS-specific data and resources used. The PHFS email listserv includes approximately 100 NGO partners, 100 country team members, and 50 government officials. It has been used ~200 times. Of these occasions, it was used ~150 times (~75%) by NGO partners, and ~50 times (~25%) by country teams. Content is representative of all categories, though the majority is external resources. NGO partners composed or re-tweeted 51 tweets using the PHFS Tiwtter. Of these, 16 (31.4%) have been external resources or data; 7 (13.7%) PHFS-specific resources; 1 (2%) PHFS-specific data; 2 (4%) PMTCT-related questions; 17 (33.3%) general updates; and 8 (15.7%) other content. PHFS has been mentioned by others on twitter 19 times: 16 times (84.2%) by partners, 2 times (10.5%) by country teams, and 1 time (5.3%) by external persons. **The** PHFS Facebook group has 60 members and 58 posts. 50 (86.2%) of these posts are from NGO partners; and 8 (13.8%) country teams. 13 (22.4%) posts are external resources, 15 (25.9%) PHFS-specific resources, 2 (3.4%) PHFS-specific data, 8 (13.8%) PHFS-related questions, 15 (25.9%) general updates, and 5 (8.6%) other content. PHFS has sent 6 email newsletters to ~250 recipients (~50 partners, ~100 country teams, ~100 others). Each email includes general updates for each (100%) country team, and external resources.

Overall, we conclude that the most effective internet-based tool to facilitate inter-country learning is the cross-country webinar, because it has resulted in the greatest amount of team-led sharing of specific PHFS- and PMTCT-related outcomes and measures.

No conflict of interest

Abstract: P_45

Prevention of Mother-to-Child transmission

A longitudinal study of the effects of HIV exposure on metabolite levels in the Midfrontal Gray Matter in children at 5 and 7 years

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Background: In South Africa, 95% of HIV-positive pregnant women and 68% of HIV-exposed infants receive antiretroviral therapy (ART). Several studies suggest that perinatal ART exposure is associated with long-term neurological effects, warranting further study of this burgeoning population of HIV-exposed uninfected (HEU) children.
Magnetic Resonance spectroscopy (MRS) is a non-invasive tool used to measure metabolite levels in the brain. Many childhood neurological processes are accompanied by metabolite changes that may correlate with demographic variables such as age. The metabolite N-acetylaspartate (NAA) is associated with neuronal density and viability, and has been observed to increase with age throughout childhood in healthy children. Choline (GPCPCh) is a marker of cellular density, and increases in choline levels are related to inflammation, myelination, or membrane breakdown or turnover; choline levels remain constant during childhood.
We investigated the relationship between age and metabolite levels in the midfrontal gray matter (MFGM) in children at ages 5 and 7, focused on HIV exposure effects.

Materials & Methods: Single voxel ^{1}H-MRS data were acquired in the MFGM on a 3T Allegra MRI Scanner (Siemens, Germany) in Cape Town, South Africa. Absolute metabolite levels were quantified using LCModel. Statistical analyses were performed in R. For expected metabolite level increase/decrease with age, a mixed effect linear regression model was used to account for repeated measures for some children.

Results: We imaged 21 five-year old (13 HEU/8 HIV-unexposed, uninfected (HUU), mean age ± standard deviation: 5.5 ± 0.4 years; 15 Xhosa/6 Cape Coloured) and 31 seven-year old (8 HEU/23 HUU, 7.3 ± 0.1 years; 24 Xhosa/7 Cape Coloured) children. All HEU children were exposed to treatment for prevention of mother-to-child transmission (MTCT).
We found a significant increase in NAA levels with age across all children (slope = 0.15, p = 0.02). HIV exposure alters the relationship between age and NAA: we find NAA increases significantly with age among HUU children (slope = 0.22, p = 0.02), but the metabolite level increase with age disappears (slope = 0.04, p = 0.6) among the HEU children.
Across all children, no difference in choline levels was observed. However, choline levels were found to increase with age *only* in HEU children (HEU (age 5): 0.95 ± 0.16 vs HEU (age 7): 1.1 ± 0.1; p = 0.03). At 7 years, HEU children have significantly higher mean choline levels than HUU children (HEU: 1.1 ± 0.1 vs HUU: 0.95 ± 0.11; p = 0.002).

Conclusions: This is the first longitudinal study to use MRS to examine HIV exposure effects on metabolite levels in children. The observed metabolite differences between HEU and HUU children in relation to age suggest brain developmental differences related to HIV exposure *in utero* and/or perinatal ART exposure.

No conflict of interest

Abstract: P_46

Prevention of Mother-to-Child transmission

HIV exposure effects on the relationship between neuropsychological measures and metabolite levels in the Basal Ganglia in 7-year-old children

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Background: In South Africa, 95% of HIV-positive pregnant women and 68% of HIV-exposed infants receive antiretroviral therapy (ART). Over the past 15 years, numerous studies have found evidence suggesting that perinatal ART exposure is associated with long-term neurological effects, warranting further study of this nascent population of HIV-exposed uninfected (HEU) children.
Magnetic Resonance spectroscopy (MRS) is a non-invasive tool used to measure metabolite levels in the brain. Many childhood neurological processes are accompanied by metabolite changes that may correlate with demographic variables such as age as well as neuropsychological measures. The metabolite creatine is found in neurons and glia, and is associated with energy metabolism. Increased creatine levels are associated with abnormal energy metabolism, and may suggest a compensatory mechanism. Choline (GPCPCh) is a marker of cellular density.
We present the relationship between metabolite levels in the right basal ganglia (BG) and neuropsychological measures at age 7, focusing on the potential effects of HIV exposure.

Materials & Methods: Neuropsychological testing and single voxel ^{1}H-MRS in the BG acquired on a Siemens 3T Allegra MRI Scanner (Siemens, Erlangen, Germany) in Cape Town, South Africa, were performed as part of an ongoing longitudinal study. Absolute metabolite levels calculated with LCModel. Statistical analyses performed in R.
The Purdue Pegboard Test (PPT) and the Kaufmann Assessment Battery for children 2nd edition (KABC-II) were performed and standard scores for the KABC-II subtests and the global Non Verbal Index (NVI) were calculated using USA norms. We performed regression analyses of metabolite measures with the PPT (preferred hand) and a select number of KABC-II scales/subtests (Sequential Processing, Learning Ability, Simultaneous Processing, and Hand Movements).

Results: Twenty-five 7-year old HIV-uninfected children, 16 HIV-unexposed (HUU) and 9 HEU, (8 girls; mean age ± standard deviation: 7.3 ± 0.1; 6 Cape Coloured/19 Xhosa) were analysed. HEU children were exposed to treatment for prevention of mother-to-child transmission (MTCT), mostly zidovudine antenatally from 28 to 34 weeks and single dose nevirapine (sd NVP) to the mother and zidovudine for a week and a sd NVP to the infant. No significant differences were found in choline levels, Hand Movement (HM) scores or PPT scores based on exposure or gender.
Mean creatine levels were significantly higher in HEU compared to HUU children (5.6 ± 0.3 vs 5.3 ± 0.3; p = 0.03), and no significant gender differences were observed.
We found an inverse linear relationship between HM subtest scores and creatine levels (slope = -3.4, p = 0.04) among all children.
In HEU children, increased choline levels in the BG are significantly associated with higher scores on the PPT (slope = 9.0, p = 0.04).

Conclusions: We observed higher creatine levels in HEU than HUU children. Among all children, creatine levels are inversely related to HM scores (visual spatial memory or motor function). A positive relationship between choline levels and the PPT (motor dexterity) was found only in HEU children. Further investigation is required to better understand the neurological basis of these differences, as well as their relationship with the underlying basal ganglia circuitry.

No conflict of interest

Abstract: P_47

Prevention of Mother-to-Child transmission

Risk of sero-conversion in the Haitian PMTCT context:Data from the National Early Infant Diagnosis Program

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Introduction: The Haitian National EID program supports over 100 sites across Haiti in the PCR diagnosis of exposed infants. When the program started in 2009, there was broad resistance amongst HIV service providers to advise HIV positive mothers to exclusively breasfed their children. This resistance was based on the risk of breast-milk transmission. Since 2008, the Haitian National recommendation has been to support exclusive breastfeeding in this population due to the reduced risk of diarrheal illness, malnutrition and infant death. Using data from the EID program we wanted to assess the potential risk of breast-milk transmission/sero-conversion in Haiti.

Material & Methods: Using the data from the National EID program (all the Hospitals enrolled except for two), we were able to tabulate the following: a) the number of 1st PCR tests; this is the total number of HIV exposed children who tested HIV negative with the first test b) the number of 2nd PCR tests; all children who tested negative with the first test require a second PCR after weaning to ensure that they have remained HIV negative throughout the breastfeeding period. c) the rate of HIV transmission for the 2nd PCR; this relates to the percentage of children who become HIV positive through the 2nd PCR after weaning .

Results: On 1108 2nd tests PCR carried on for previously negative exposed children from 2011 to 2013,data shown that 619 were breastfed (49.2%). 23 of the 619 tested positive after weaning with a percentage of seroconversion varying from 1.27% , 2.9% and 3.5% per year.

Conclusions: Through recording the number of first and second PCR tests, the number of second PCR is significantly less than the number of first PCRs.Nonetheless, for the children breastfed we deem this transmission rate low and therefore consider it appropriate to promote exclusive breastfeeding given the risks associated with formula.

No conflict of interest

Abstract: P_48

Prevention of Mother-to-Child transmission

HIV Exposed Infant Cohort Analysis: Results from an Innovative Method for Routinely Monitoring Longitudinal Outcomes of HIV Exposed Infants, Kenya

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Background: Globally, mother to child HIV transmission (MTCT) has reduced by 35% since 2009. Despite this reduction, 260,000 infants were infected in 2012, 13,000 (5%) from Kenya. While virologic laboratory testing data are available to track early infant diagnosis, less is known regarding HIV-exposed infant (HEI) follow-up through the recommended 18-month period. To address this gap, the Kenya Ministry of Health (MOH), with support from U.S. Centers for Disease Control and Prevention-Kenya, implemented a HIV Exposed Infant Cohort Analysis (HCA) system to assess Prevention of Mother-to-Child Transmission (PMTCT) outcomes towards the elimination target of reducing MTCT to <5%.

Methods: Health facilities began routinely implementing the HCA system in July 2013, with 1,275 (27%) of Kenya's 4,761 PMTCT sites reporting by December 2013. On a monthly basis, trained health care workers abstract aggregated birth cohort data from the MOH HEI longitudinal register to assess nine- and eighteen-month infant outcomes and service uptake. Using frequencies, we analyzed data submitted from July-December 2013, which reported nine-month outcomes for infants born in July-December 2012 and eighteen-month outcomes for infants born in July-December 2011.

Results: Among the 11,747 infants assessed by age nine months, 10,474 (89%) had received prophylactic antiretroviral drugs; 9,295 (79%) were tested for HIV by two months, of whom 339 (4%) were HIV-infected. An additional 205 (2%) were identifed positive by nine months for a total of 544(5%) infected infants, of whom 451 (83%) were enrolled in HIV care. By nine months, of the total 11,747, 1,318 (11%) were lost to follow up and 234 (2%) had died. Among the 11,238 infants assessed by age 18 months, 7,038 (63%) were HIV-negative, 740 (7%) were infected, 1,751 (16%) were lost to follow up, and 383 (3%) died. Of the 740 identified positive, 617 (83%) were enrolled in HIV care.

Conclusion: Preliminary HCA results highlight achievements in early infant testing and prophylaxis coverage and challenges in reducing MTCT to <5%, ensuring linkage to care, and retaining infants up to 18-months. Continued scale-up and integration into the national health information system is ongoing, which is expected to inform facility, county, and national PMTCT improvement efforts.

No conflict of interest

Abstract: P_49

Prevention of Mother-to-Child transmission

Effectiveness of Prevention of Mother-to-Child Transmission (PMTCT) Program at Six Weeks Postpartum in Rwanda within one year implementation of Option B/B+

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Introduction: In November 2010, Rwanda adopted 'Option B' of the 2010 WHO recommendations for the use of ARV in Prevention of Mother to Child Transmission of HIV (PMTCT) before shifting to Option B+ in April 2012. All HIV-positive pregnant women now receive lifelong triple therapy. This is the first study to examine early mother to child transmission of HIV (MTCT) in the context of the Rwanda Option B/B+ PMTCT program.
The aim of the present evaluation is to measure the population-level effectiveness of the PMTCT program in Rwanda. The primary objectives of the study were to measure rates of early mother to child transmission (MTCT) of HIV at 6-10 weeks postpartum, and to estimate coverage of key PMTCT interventions and services.

Materials & Methods: From June 2011 until June 2012, a cross-sectional survey was conducted. Stratified multi-stage, probability proportional to size (PPS) and systematic sampling methods were used to select a representative national sample of infants aged 6-10 weeks and their mothers/legal guardians. Trained health care staff conducted interviews in privacy at the health centers and infant dried

blood spot (iDBS) samples were collected by trained laboratory technicians from infants of consenting mothers/legal guardians.
Eligible infants included those with known HIV-positive mothers, HIV-negative mothers living with a sero-different partner or a partner whose HIV status was unknown, or mothers whose HIV status was unknown. To identify HIV status of mothers, HIV rapid test was performed on eligible mothers except known HIV-positive mothers. For infants of all HIV-positive mothers an iDBS PCR was performed. For eligible mothers who refused to be tested for HIV but consented for participation of the infant or for infants whose mother was absent or dead and the legal guardian provided consent, an iDBS sample was also collected. The desired sample size was 2042 infants from 161 health facilities. iDBS PCR testing was conducted centrally by the National Reference Laboratory (NRL). We conducted univariate and multivariate analysis using STATA 10.9 Corp, and accounted for survey characteristics.

Results: The realized sample for the study was 1639 completed interviews of mothers of HIV-exposed infants with confirmed iDBS results, which is 82% of desired sample size of 2042.
Twenty-six infants were diagnosed HIV-positive on DNA PCR from DBS. This translates to a weighted overall early MTCT in infants up to 6-10 weeks of age of 1.58% (95% CI 1.05%-2.37%).
Uptake of key PMTCT program indicators such as HIV testing, CD4 count testing, and maternal HAART during pregnancy were above 90%. Referral to ART clinic, disclosure of HIV status and infant feeding counseling ranged from 80%-90%. 96.6% of HIV-exposed infants received ARV prophylaxis. The combined indicator for maternal HAART and infant ARV prophylaxis according to Rwanda national B/B+ protocol was 90.4 %.

Conclusions: Rwanda has rolled out Option B+ to most mother-infant pairs and achieved an MTCT rate of 1.58% at 6-10 weeks. However, given high breastfeeding prevalence, further studies are needed to assess the contribution of the new regimen (Option B+) to long-term effectiveness of the PMTCT program.

No conflict of interest

Abstract: P_50

Complications of HIV therapy

Antiretroviral exposure during pregnancy and assessment of neurological conditions in HIV-exposed/uninfected infants: Data from the NICHD NISDI cohort

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Introduction: Among HIV-exposed/uninfected (HEU) infants there is concern that neurologic conditions (NC) may be more frequent among those exposed to particular antiretroviral drugs (ARVs).

Materials & Methods: The NICHD International Site Development Initiative (NISDI) is a prospective cohort study of HEU infants from 24 clinical sites in Latin America and the Caribbean that collected data on maternal demographics, health, HIV disease status, and ARV use during pregnancy. Infant data included head circumference after the newborn period and medical diagnoses at birth, 6-12 weeks and 6 months. Only infants with maternal exposure to combination ARV (cARV) (defined as 3 or more drugs from at least 2 classes) during pregnancy were included in this analysis. Outcomes of interest were microcephaly (WHO head-circumference for age z score < -2 standard deviations) and neurologic conditions (NC) (microcephaly,

neurologic diagnosis, lactic acidosis diagnosis, neuro-ophthalmologic conditions or mitochondrial disorders). Logistic regression was used to determine the association between the outcomes and specific ARV exposure and to investigate other potential covariates associated with microcephaly or NC.

Results: From 2002-2009, in 1400 eligible HEU infants, NC were reported in 134 HEU infants (9.6%, 95% CI: 8.1%, 11.2%) including 105 cases of microcephaly. The most common maternal ARVs used during pregnancy were 3TC (98.1%), ZDV (94.2%), NFV (40.6%), LPV/r (28.4%), and NVP (35.9%). No cases of lactic acidosis or mitochondrial disorders were reported. The odds of microcephaly or NC were not significantly associated with any specific maternal ARV, trimester of cARV initiation, CD4+ cell count or viral load during pregnancy. Covariates significantly associated with increased odds of NC included male sex (OR 1.93), birth weight < 2.5 kg (OR 3.15), non-infectious obstetric complications (OR 1.82), congenital infections (OR 2.27), and 1-minute Apgar score < 7 (OR 2.60).

Conclusions: This is the first study assessing microcephaly among HEU infants exposed to ARVs *in utero*. Among cARV exposed HEU infants from Latin America and the Caribbean, no individual maternal ARV was significantly associated with microcephaly or NC. Anticipated infant and maternal factors associated with higher odds of microcephaly and NC highlight the need for interventions to reduce these complications among pregnant women with HIV infection.

No conflict of interest

Abstract: P_51

Complications of HIV therapy

Anemia in neonates born to HIV-Infected Women: the role of G6PD Deficiency and Zidovudine Exposure

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Background: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common hereditary enzymopathy, particularly frequent in sub-Saharan Africa. Intravascular hemolysis necessitates a trigger. We aimed to determine the role of zidovudine exposure, in utero and during the first month of life in the occurrence of anemia in children born to HIV-infected mothers.

Methods: We conducted a retrospective monocentric study including all neonates born to HIV-infected women in a single tertiary academic hospital center (Colombes, France) between 2005 and 2013 and enrolled in the French Perinatal Study (ANRS-EPF-CO1). HIV-infected children were excluded. All neonates were tested for G6PD deficiency. Anemia, graded according to the PACTG classification was evaluated at birth, one month and 3 months for all children. Associations between anemia, G6PD deficiency and zidovudine exposure were studied with Chi2 tests and multivariate logistic regression.

Results: Among the 383 children included, 12% had G6PD deficiency, 11.2% were born preterm and 17.5% had a birthweight < 10th centile. All newborns received prophylaxis with zidovudine for 4 to 6 weeks. There was a trend towards more frequent anemia at birth for children with G6PD deficiency: 44% vs 30%, p = 0.06 but no difference in severe anemia (grade 3-4) : 11% vs 10%, respectively. At 1 month, the difference was greater and reached significance: anemia 76,1 % vs 53,4 % (p=0,004) with grade 3-4 anemia 11% vs 1% (p< 0,001). In multivariate analysis adjusting in particular for gestational age and birthweight, in utero exposure to zidovudine was significantly associated with anemia at birth, AOR=3.2 ; 95% CI [1.5-6.9], p=0.02, but not at 1 or 3 months. This association was independent from G6PD deficiency which was significantly associated with anemia at birth, AOR=2.1 [1.1-4.0], at one month, AOR=2.9 [1.4-6.0], but not at 3 months. There was no interaction between G6PD deficiency and zidovudine in utero.

Conclusion: Anemia in newborns exposed to zidovudine in utero has been previously

reported and children born to HIV-infected women of sub-Saharan origin are also at risk for G6PD deficiency. The concurrent effect of zidovudine and G6PD deficiency has not been studied previously. We found no interaction, but both are significantly associated with anemia at birth, leading to a high prevalence in those neonates exposed to both risk factors. Screening neonates for G6PD deficiency is important in order to prevent the occurrence of severe anemia in this high-risk population.

No conflict of interest

Abstract: P_52

Complications of HIV therapy

Implementing D4T phase out in children taking ARVs in Swaziland'

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Background: From inception of the Swaziland ART program, treatment for children was a priority and availability of pediatric ART formulations shaped the prescription patterns. In 2008 the Ministry of Health MoH introduced the first pediatric generic fixed dose combination (FDC) available in the market, based on Stavudine (d4T) in an effort to phase out the use of syrups formulations. The easy forecasting, storage and use made it an essential tool to provide treatment to children and facilitated access to treatment and long-term adherence. The Zidovudine (AZT) based pediatric FDC was made available in 2010 and from then the country could direct efforts at decreasing the use of d4T to limit long-term exposure to related side effects and align with current WHO recommendations. In comparison, d4T consumption in adults was never so significan as first line regimne was based on AZT.

Material and Methods: We reviewed retrospective routine program data for ART prescription in children (<15 years) and adults (>15 years) for the years 2011 to 2013. Data was extracted from routine programmatic reports containing pediatric ART aggregated consumptions, located at the Swaziland Central Medical Stores (CMS). Absolute numbers and trends were collected. Also, we documented the process of d4T phase out in the country overall and focused on the pediatric population over time.

Results: Consumption data from the Swaziland Central Medical Stores (CMS) shows that in 2011, out of the 2156 recorded chilren, 44,4% (957) of them where using the D4T-based pediatric FDC and this proportion drops to 28% at the end of 2012 and to 22% by the end of 2013. This compares with consumption of d4T in adults at 8.9% in 2011 to 0.8% at the end of 2013. Program efforts still consider d4T phase out as a priority for the national program in 2014 and multiple efforts are directed to rationalize the use in the pediatric population according to the country guidelines.

Conclusions: Phase-out of d4T-containing products required strong coordination and collaboration between policy makers, implementing partners, CMS, pharmacists and medical personnel at country level. Treatment guidelines and implementation of the phase out plan in Swaziland was undertaken with detailed preparation, including robust forecasting down to the facility-level, and preparation of facility-level plans for patient transition, as well as capacity building and sensitization of health care workers and continued monitoring and evaluation of the process.Policy makers and implementers must direct special efforts to decrease d4T consumption in national ART programs.However d4T may continue to play an important role in ART care of children in Swaziland, as compared to adults, until a viable alternative regimen is available in the country in the coming years.

No conflict of interest

Abstract: P_53

Co-infections in HIV-infected children

Immunogenicity of a booster dose of MCV4 in previously immunized HIV infected children and youth

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Background: The US Advisory Committee on Immunization Practices recommends a booster dose of quadrivalent meningococcal conjugate vaccine (MCV4) five years after initial immunization for patients at high risk of meningococcal infection, including those with HIV infection. There are no published data regarding the immunogenicity of a booster dose of MCV4 in HIV-infected children and youth.

Methodology: IMPAACT P1065 was a safety and immunogenicity trial of MCV4 in HIV-infected youth and children at 32 IMPAACT sites in the U.S. The final step was an open-label study of a booster dose of MCV4 given at 3 years +/- 6 months after a single or two-dose (with 6-month interval) primary MCV immunization. There were two groups of participants: those 11-24 years old (youth group, YG), CD4% ≥ 15% at the time of initial immunization, and those 2-10 years old (pediatric group, PG), CD4% ≥ 25% at time of initial immunization. Antibody titers were evaluated at time of booster vaccine dose and 1, 4, and 24 weeks post-booster. Immunogenicity was measured by rabbit serum bactericidal antibody (rSBA) against each meningococcal serogroup (SG) (A, C, Y, and W-135). The primary objective was to evaluate the rates of memory and primary response after the booster dose. Memory response was defined as either seroprotection (rSBA titers > 1:128) or a ≥4-fold increase at week 1 after the booster dose. Primary response was defined as either ≥4-fold response or being seropositive at week 4 in the absence of a memory response. Adverse events (AE) were assessed for 4 weeks after the booster dose.

Results: Of 174 participants (138 YG, 36 PG) who had serology results at weeks 0, 1, and 4, 66% had a viral load of <400 copies/mL at the time of entry to this step, 89% were on ART, 58% were male, and 51% African American. Memory response to at least one SG occurred in 98% of participants: 93% for each of SGs A and Y, 88% for SG C, and 94% for SG W-135; 83% had memory responses to all four SGs. The memory response rates were similar whether the primary series was one or two doses of vaccine. Primary or memory response occurred in 95% of participants for SGs A and W-135, 90% for SG C, and 96% for SG Y. Only 4 participants lacked a memory response to at least 1 SG, and only 2 did not have primary or memory response to any SG. At week 0, 26%-69% of patients had protective rSBA titers to the various SGs; this increased to 87%-93% at one week post-immunization. There were no serious AEs within 42 days after the booster dose.

Conclusions: A booster dose of MCV4 in previously immunized HIV-infected children and youth elicited memory responses in 88%-94% of participants, varying by SG, and resulted in significant increases in seroprotection against all meningococcal SGs, even in participants lacking protective titer levels pre-booster vaccination.

Conflict of interest: MD Decker is an employee of Sanofi Pasteur. SA Spector holds stock in Sanofi Pasteur.

Abstract: P_54

Co-infections in HIV-infected children

Uptake and outcomes of HCV treatment in children and young adults with HIV/HCV co-infection in Europe

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Introduction:There are scarce data about anti-HCV therapy in HIV/HCV co-infected children. We explored current uptake and outcomes of HCV treatment in children and young people with HIV/HCV co-infection in Europe.

Materials and Methods: We performed a retrospective, cross-sectional study, within 11 European paediatric HIV cohorts in 2012-2013. Patients aged <25 years, with HIV/HCV acquired vertically or in childhood, were included.

Results: Of 225 subjects identified with HIV/HCV co-infection, 55 (24%) received HCV treatment (peginterferon alfa / ribavirin), of whom 38 (69%) were female. Median age at treatment start was 17.2 years (min, 3.5; IQR 9.9,22.2); 12 (22%) had a history of AIDS and 47 (85%) were receiving ART. Uptake of HCV treatment varied between countries: 61% (30/49) patients were treated in Russia, 37% (6/16) in Italy, 33% (1/3) in Belgium, 26% (12/46) in Spain and 9% (6/67) in Ukraine; no treatment was given in Germany, Poland, Romania, Switzerland or the UK/Ireland. Forty-four of the treated patients had results of transient elastography (TE) available: 17 (39%) had liver fibrosis equivalent to Metavir ≥F2 (>7.3 kPa), including 8 (19%) with severe fibrosis or cirrhosis. Factors associated with treatment uptake were GT2/GT3 (AOR 2.5, 95%CI 1.1, 5.7, versus GT1/GT4) and age 18-24 years (AOR 3.9, 95%CI 1.4, 11.4, versus 11-17 years), after adjusting for TE and mode of acquisition. Overall, 55 (24%) patients received HCV treatment (peginterferon alfa + ribavirin). Thirty four (62%) had outcome data available on virological response at 24 weeks after end of treatment (SVR24): SVR24 was 33% (6/18) for GT1 and 70% (7/10) for GT3; the 1 GT2 patient had an SVR24 and 1 of the 2 patients with unknown GT; not one of the 3 patients with GT4 achieved SVR24.

Conclusions: HCV treatment in HIV/HCV co-infected youth varied across Europe. Patients >18 years and those with GT2/GT3 were more likely to be treated. We show substantially lower SVR24 rates compared to the studies of HCV mono-infected children and adults. With new antivirals promising better outcomes in HCV mono- and HIV/HCV co-infected adults, there is an urgent need to initiate clinical trials in this population.

No conflict of interest

6th International Workshop on HIV Pediatrics

Abstracts
Abstract Book only

Abstract: A_01

Treatment of pediatric HIV infection

Children living with HIV in Ukraine: response to antiretroviral therapy(ART) and duration of first-line regimens

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Introduction: Ukraine has one of the fastest growing HIV epidemics in the world, with considerable unmet need for treatment among the adult HIV-positive population. Research into the health and treatment of HIV-infected children in this lower middle-income country, or indeed elsewhere in Eastern Europe, has been limited to date.

Material & Methods: The Ukraine Paediatric HIV Cohort Study is a consented cohort enrolling in HIV/AIDS Centres in Kiev, Odessa, Donetsk, Mykolaiv, Mariupol and Simferopol. Children and adolescents aged up to 18 years old, with confirmed HIV infection (regardless of mode of acquisition) being cared for at these centres are eligible for enrolment. At enrolment, anonymised retrospective and current visit data are collected, following medical note review dating back to HIV diagnosis, with follow-up data collected at subsequent clinic visits. Data on children on antiretroviral treatment (ART), recruited by March 2013 were analysed. Second-line ART was defined as change of ≥3 drugs simultaneously irrespective of reasons or changing 2 drugs due to treatment failure. Factors associated with switch to second-line ART were explored with Cox proportional hazards models.

Results: Of the 649 children on ART, 99% had acquired HIV vertically, 50.1% were female and 99.5% were born in Ukraine. Median age at enrolment was 6.8 years (range, 1 month–17 years); 38% (n=237/619) had a prior AIDS diagnosis; current WHO clinical staging was 1: 5% (n=32), 2: 42% (n=248), 3: 33% (n=195) and 4: 19% (n=115) (59 missing). Four percent (26/649) of children were HIV/HCV co-infected and 1% (7/649) were HBsAg positive. Median age at ART initiation was 52.4 months (IQR 28.8, 78.6) and 8.4 months (IQR 4.3, 24.1) among children born before and after 01/01/06 respectively.
Of treated children, 62% (n=425/649) were on their first regimen, most commonly Kaletra-based with a 3TC+ZDV backbone. Overall 15% (n=100) treated children had switched to second-line regimens, while 19% (n=124) had experienced ≥1 drug substitution(s). For children on first-line regimens, median time since ART initiation was 33 months (IQR 11, 64); median duration of first-line regimen among children on second-line regimens was 16 months (IQR 9, 33). Adjusting for sex, centre, WHO stage, age at HIV diagnosis, baseline CD4% and viral load before switch, factors associated with time to switch to second-line ART were CD4% at baseline (aHR 0.98, p=0.047 per unit increase) and viral load (aHR 0.30, p<0.01 for viral load <400 copies/ml vs. viral load >400 copies/ml).

Conclusions: Age at ART initiation among HIV-positive children in Ukraine has substantially decreased over time, reflecting implementation of early infant diagnosis and ART roll-out. There appears to be good durability of first-line regimens in this setting.

No conflict of interest

Abstract: A_02

Treatment of pediatric HIV infection

Host genes associated with slow disease progression among perinatally-infected Indian children

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Introduction: Understanding the genetic background of HIV-infected subjects and the impact of host genes on disease progression would increase our collective predictive ability of disease evolution. Reports of perinatally-infected children who are 'slow progressors' with a median survival of 16 years or more without ART have spurred us to explore specific host genetic factors and their impact on disease progression in this population.

Materials and methods: Among a cohort of 165 HIV-1 infected children in Bangalore, India, we identified 6% (10/165) long-term non-progressors (ART-naïve, HIV-1 infection for ≥10 years and CD4 cell count ≥500 cells/mm3), 5% (8/165) slow progressors (ART-naïve, HIV-1 infection for≥10 years and CD4 cell count ≤500 cells/mm3), and selected 5% (8/165) normal progressors on ART. Among these children, we tested the host genes, CCR5-?32, SDF1-A, CCR5-59029G using allele-specific PCR-RFLP, and HLA-B*27 and B*57 using SSPGo HLA typing kits.

Results: Among the 30 study subjects, 14 (46.6%) were male. Median CD4 count was 375 cells/mm3 (IQR: 246-636;) and mean viral load, 5.3 (±0.7) log copies/ml. None of the children had CCR5?32 deletion. Frequencies of SDF1-A and CCR5 59029G in 30 children were 17% and 50% respectively. HLA-B57 polymorphic allele was found in two children; one among slow progressors and one among long-term non-progressors, while HLA- B27 was also found in one slow progressor.

Conclusions: The results from this first-time Indian study investigating the dynamics of host genetic factors among differentially progressing ART-naïve children indicated a possible combined effect of HLA class-I alleles with other chemokine receptors and their ligand polymorphisms that may predict HIV disease progression. Ongoing longitudinal studies can elucidate this specific effect in more detail.

No conflict of interest

Abstract: A_03

Comprehensive Pediatric HIV care

Observation of resolved lower limb tone abnormalities in children with HIV encephalopathy on antiretroviral treatment

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Introduction: Human immunodeficiency virus (HIV) in children can cause central nervous system impairments of which HIV encephalopathy (HIVE) is the most common clinical presentation. About 60% of children attending an HIV-Neurology clinic at Red Cross War Memorial Children's Hospital in Cape Town, South Africa were diagnosed with HIVE, of which 63% presented with increased muscle tone in the lower limbs. Increased muscle tone in the lower limbs and associated abnormalities in gait pattern are characteristic of spastic diplegia, a condition well-described in children with Cerebral Palsy. However, whereas Cerebral Palsy is a non-progressive disorder, it is unclear whether increased muscle tone is stable or progressive over time in children with HIVE, who are on anti-retroviral treatment (ART). Therefore, the aim of this study was to investigate changes in muscle tone in the lower limbs at least 6 months after the initial HIVE diagnosis, in children with HIVE receiving ART.

Material & Methods: Participants were selected from a database of children who had attended an HIV clinic at Red Cross War Memorial Children's Hospital between 2008 and 2013 and fulfilled strict selection criteria including a diagnosis of HIVE with spastic diplegia or increased muscle tone with brisk reflexes in the lower limbs. The follow-up measures included assessment of muscle tone in the lower limbs and visual inspection of the child's walking and running gait.

Results: The study-cohort consisted of 16 children (6 female, 10 male), with a mean age of 5.7 ± 2.7 and 8.5 ± 1.8 years at the initial-

and follow-up- assessments, respectively. Eleven children no longer showed any evidence of increased muscle tone at the follow-up assessment (mean follow-up time 2.4 ± 1.6 years), either during the physical examination or during visual inspection of the child's walking and running gait (Group A). Five children continued to show increased muscle tone and a typical spastic diplegic gait pattern in the follow-up assessment (mean follow-up time 3.3 ± 2.2 years) (Group B). An unpaired t-test showed no significant differences in age at the initial assessment (p=0.37) or the follow-up time between assessments (p=0.35) for Groups A and B. The groups did, however, show a difference in the severity of the initial neurological findings; the children in Group B were specifically described as spastic diplegic in the initial assessment whereas this was not the case for the children in Group A.

Conclusions: Our observations suggest that increased tone in the lower limbs in children with HIVE may resolve over a period of months or years on standard ART regimens. However, children presenting with spastic diplegia do not seem to show the same improvement over time. Although further investigation of the natural history of HIVE and spastic diplegia is required to confirm these findings, the current observations may be of immediate relevance to healthcare professionals who may wish to consider the current findings when assessing the prognosis and treatment options for children with HIVE who present with increased tone in the lower limbs.

Abbreviations: HIVE: human immunodeficiency virus encephalopathy
ART: Anti-retroviral treatment

No conflict of interest

Abstract: A_04

Comprehensive Pediatric HIV care

Entire family in the boat moving with turbulence: family caretakers' experiences of caring for a child with HIV on Antiretroviral therapy in Ethiopia

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Background: Family care givers play a critical role in caring for children living with HIV but there is little information on their lived experiences. This preliminary finding is part of a longitudinal study aimed at illuminating the family caretakers' experiences of caring for a child living with HIV when a child was diagnosed with HIV and enrolled to antiretroviral treatment.

Method and design: We conducted in-depth interview with eight family care givers and inductive qualitative assessment using a hermeneutic phenomenological approach. The interview with tape record was transcribed in local language and then translated to English. Finally, we analyzed data thematically.

Results: Eight family care takers/children pair enrolled in the study. The family care givers experiences were articulated in seven themes under the main theme of *'Entire family in the boat moving with turbulence'.*
In the beginning when a child tested HIV positive, the family life is *'Breaking family life'.* The entire family of the child with HIV felt that they faced a disaster in the family which put the entire family life in desperation and the family fabric loosen. Biological parents felt as criminals as they were the reason for the HIV status of their child which was acquired through vertical transmission. Their child's positive HIV status is disturbing them where at times they get panicked and condemned themselves resulted in ***'Self-**blaming and guilty feeling'.*
The other family care givers experience includes facing *'Dilemma with child's Curiosity'.* Children with HIV want to know that why they are taking the treatment and for how long. This condition puts the family care takers in dilemma and confusion, and put them in a lot of pressure about how to respond to this situation. Family care givers challenge continued with *'Complexity of care and peculiar*

prerequisites' to fulfil the child's holistic needs with requirements related to keeping his/her treatment protocol and follow up at home.
It is very difficult for family care givers to accept just a child has to start and continue the treatment through his/her life time. But on the other hands the future hope on the treatment, health providers advise and their empathetic approach created the care givers to have good feeling and which ultimately put them to have bidirectional feeling of *'Combination of dejection and Bloom'* despite *'Struggling with ambiguous imminent'* when they think about their child's future. Most of the care givers didn't want their child status to be open to others due to the feeling of *'Jeopardy of being revealed'.*

Conclusion: Initial HIV diagnosis, initiating the child on lifelong treatment, and the ambivalent future of the child put the family caregivers' life through moments of broken family, frustration, and misery. Some light of hope comes with the treatment and health workers support during child's treatment initiation. The health care system should be prepared to support family care givers during child's HIV diagnosis and treatment initiation as part of continuum of care beyond the support being provided at health facility level.

No conflict of interest

Abstract: A_05

Comprehensive Pediatric HIV care

Patterns and predictors of adherence to antiretroviral therapy among children living with HIV in India

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Background: Antiretroviral treatment (ART) has markedly improved survival in HIV-infected children. Adherence to ART is fundamental to treatment success, although this has been poorly studied in India. This cross-sectional study aimed to measure ART adherence, understand barriers and predictors of adherence in HIV-infected children receiving care under the national AIDS control program of India.

Materials and methods: Caregivers of children attending HIV clinics at three tertiary-care centres in Karnataka state were interviewed using structured questionnaires. Adherence was assessed using a visual analogue scale (past month adherence) and self-reported treatment interruptions over the past 3 months. Optimal adherence was defined as adherence ≥95% in the past month. Clinical features and viral load measurements were documented. Statistical analyses, including frequency distributions, chi-square and correlation tests were performed using SPSS.

Results: A total of 247 children with their caregivers participated in the study. The mean age was 9.82±3.47 years, 57.5% were males, and 83.3% were in WHO Clinical Stage 1 or 2. Mean duration of ART was 25 months. Among 164 children on ART, 90.9% were optimally adherent, and treatment interruptions >48 hours were reported by 4.9%. Factors associated with suboptimal adherence included unwillingness to medicate in front of others (p=0.04), and inability to reach the provider clinic on time (p=0.01), leading to missed appointments (p=0.01). The proportion of children with detectable viremia was 20.7%. The distribution of virological failure was similar among children who were suboptimally and optimally adherent (26.7% and 19.6%, respectively, p=0.74). There was no association of adherence between those who were partially or fully disclosed compared to those who were unaware of their diagnosis.

Conclusions: Adherence to ART among children attending the ART centers under the national AIDS control program is high. Challenges to achieving optimal adherence include stigma and difficulties in accessing provider facilities. In a setting of relatively high adherence, factors influencing virological failure need further study. Emphasis on access to care, provision of nurse-based and caregiver-support services, and programmes aimed at decreasing stigma could improve overall outcomes in pediatric HIV.

No conflict of interest

Abstract: A_06

HIV infection and adolescents

Knowledge and attitude of adolescents towards HIV/AIDS- a cross sectional study

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Introduction: Adolescents form a sizeable portion of the Indian population. In India, AIDS prevention and control efforts remained largely concentrated on groups already practising high-risk behaviour (like commercial sex workers, iv drug abusers, long route drivers etc.). Thus other potential groups like older school children, adolescents and younger adults, who because of their vulnerability deserve simultaneous attention, continue to remain a low priority

Methods: The present study was carried out to assess the level of awareness among school and college going students between the ages of 14-19 years about HIV/AIDS in Guwahati, Assam, a city in the north eastern part of India .500 adolescents were given a pretested questionnaire on random basis and requested to fill it up and return within half an hour .
The data was analysed manually using tally mark method and also subjected to Chi Square test of independent analysis and proportion test wherever needed. A p value <0.05 was considered statistically significant.

Results: The main source of HIV/AIDS awareness was media. Very little communication regarding HIV/AIDS occurred between the teenagers and their parents and teachers, representing that matters pertaining to sex, sexuality and reproduction still continue to be a taboo in our society. This study reveals good awareness about modes of transmission and prevention, although the awareness regarding homosexual route (42.4%) and breast milk as possible routes of transmission (58%) was less among the study population. Misbeliefs on the modes of transmission of the disease like through handshake, kissing, use of fomites was close to 30% . There is also a minor discrepancy between knowledge and attitude. Though majority of the study population had a good knowledge of HIV/AIDS, a substantial portion (20-30%) demonstrated negative attitude towards HIV/AIDS victim. Thus knowledge alone doesn't seem to be enough to change attitude towards HIV/AIDS victim.

Conclusion: A more appropriate programme based on behavioural science is desirable to lessen discrepancies between knowledge and desirable attitude. Implementation of HIV/AIDS awareness programme in schools and colleges and community, as well as adolescents outside educational institutions need to be covered by voluntary organisations, NGO s etc. in collaboration with National AIDS Control Organisation.

No conflict of interest

Abstract: A_07

HIV infection and adolescents

Importance Of ARV Adherence Driving Paediatric HIV Disclosure: Experiences Of Parents Of 7-12 Year Old Children In Kampala, Uganda

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Background: The estimated 2.8 million children < 15 years living w ith HIV in sub-Saharan Africa are surviving into adolescence due to increased availability of antiretrovirals (ARVs) and improved care. Disclosure of HIV diagnosis to children by age 12, as recommended by WHO, remains low (5-30%) despite evidence of positive effects. Detailed information about disclosure process and outcomes can inform the design of culturally and developmentally appropriate interventions

that respond to the needs of parents and children.

Methods: Between August and October 2013, parents of HIV-infected children (7 to 12 years) old receiving care at an HIV clinic w ere consecutively recruited into a cross-sectional study assessing pediatric HIV status disclosure prevalence, parent reasons for disclosure or nondisclosure, and parent experiences of their own and their child's disclosure. We used mixed methods to examine disclosure processes and outcomes from parent interviews.

Results: 22/66 parents reported having disclosed the child's HIV status to the child. 22/69 children received full disclosure (HIV mentioned) while 1/69 partial disclosure. 50% of parents disclosed after their child's questioning or refusal of daily ARV consumption. Parents who prepared children showed them affection, talked about HIV in general, or gave the child a treat. The majority of disclosure conversations centered on the importance of lifelong ARVs - ranging from the threat of death to the potential for bright futures as a consequence of defaulting or adhering respectively. 'We asked her what she wants to be in future, she said . . . a doctor, so we told her if you take the drugs you will be able to study and achieve your dream.' Many parents opted to share their own HIV-status with their child during the conversation and the majority described a sense of relief after disclosure. Better ARV adherence was largely reported following child's understanding of the reason for taking the drugs

Conclusions: Parents of HIV-infected children are aware of the critical importance of ARV adherence which seems to drive the child´s HIV status disclosure to the child. Further investigation is required to determine how this can be incorporated into interventions /policies to support and facilitate HIV diagnosis disclosure to children.

No conflict of interest

Abstract: A_08

Implementation research on PMTCT and pediatric treatment programs

Retention in Care of a Mother-Infant Cohort Enrolled in an Integrated Prevention of Mother-to-Child Transmission (PMTCT) and Maternal and Child Health (MNCH) Program

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Background: Separate antenatal and HIV services limit opportunities for optimal delivery of PMTCT services, rendering follow -up of HIV-infected mothers and their infants a challenge. Integrated PMTCT, maternal, newborn and child health (MNCH) services have been promoted but not well studied. We report on retention of mother-infant pairs up to 18 months post-partum and infant testing outcomes in a prospective cohort enrolled in an integrated PMTCT/MNCH service in South Africa. Services included primary health care, immunizations, comprehensive HIV care and antiretroviral treatment (ART), infant and partner HIV testing, infant feeding, growth and developmental assessments, psychosocial support and reproductive health services.

Methods: HIV-positive, pregnant women ≥18 years enrolling from January, 2010 were followed with their infants to 18 months post-partum. Women received ART for life/ PMTCT or AZT and sdNVP. Data were collected on maternal obstetric and infant outcomes, morbidity and mortality, retention in care and reasons for exit ≤18 months.

Results: 175 women (median age 30) were enrolled between 2010-2011 (Figure). Median follow - up time from enrolment was 20.2

months (IQR 8.8-22.9). 168/174 infants (97%) were tested for HIV by PCR at 6 weeks, 1.2% were HIV-antibody positive. Of the 166 infants who tested HIV-negative at 6 weeks, 101 (61%) remained in care at 18 months; 93 (92%) were tested for HIV by rapid test, 1 (1%) was HIV-antibody positive. Of the 77 mothers who left the cohort ≤18 months, 53% left to access care elsewhere for financial reasons, relocation, or work requirements. 36 (21%) mothers with their infants were lost to-follow-up over 18 months.

Conclusions: Integration of PMTCT and MNCH services is a promising strategy for effective delivery of interventions to mother-infant pairs. To optimise PMTCT coverage and improve uptake of infant testing at 18 months, it is important to better understand the time periods of greatest attrition and reasons for exit of current care.

No conflict of interest

Abstract: A_09

Prevention of Mother-to-Child transmission

Evaluation of the CCCRN Sample Referral System (SRS) for Early Infant Diagnosis (EID) in the Prevention of Mother to Child Transmission (PMTCT) program in Nigeria

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Introduction: The National PMTCT and Early Infant HIV Testing Policy of Nigeria recommends HIV testing for infants by dried blood spot (DBS) DNA PCR from 6 weeks of age and rapid test at 18 months. This is to allow for early diagnosis and treatment. However, one of the major factors affecting the EID for PMTCT is distance to the PCR testing laboratory and the long turnaround time. In order to close this gap, the Centre for Clinical Care and Research in Nigeria (CCCRN) laboratory program emanated an efficient system to deliver timely testing and treatment to the exposed infants in the PMTCT program called Sample referral system (SRS). This was a revised protocol on how to improve the logistics of EID sample/result delivery and support the PMTCT Program. The objectives of this evaluation were to assess: 1) the effectiveness of the CCCRN SRS for EID in the PMTCT Program, 2) use of internal courier system for controlled turnaround time, 3) feasibility and quality aspects of DBS-PCR in our setting.

Method: In this prospective cohort evaluation, 528 HIV-exposed infants' DBS samples (from October 2013 to March 2014) were monitored from CCCRN supported sites in Enugu State.

Results: Using the CCCRN SRS, 63.8% (337/528) of DBS samples have received results with an average turnaround time of 2 weeks. 35.2% (n=186) have not yet received results at the moment. 52.7% (n=278) of these were tested at 6 weeks for PCR one, while 33.7% (n=178) were tested for PCR one at more than the recommended 6 weeks of age. 13.6% (n=72) of those were tested PCR two. 0.95% (n=5) of DBS samples were rejected and did not receive results because of poor collection quality while and the overall mortality rate was 0.2% (n=1).

Conclusion: The reported turnaround time is acceptable to the National PMTCT EID turnaround time of between 2-4 weeks. The biweekly centralized sample storage and dispatch not only has it abbreviated the turnaround time from over 6 weeks to only 2 weeks, it has reduced loss of DBS samples due to poor storage at sites and improved early treatment for the HIV positive infants. This has also improved the central collation of data (number of samples delivered, results received, and with respect to time). This system has mostly saved cost as samples are dispatched in bulk and results collected the same day samples are dispatched. Sample rejection due to poor quality of specimens reinforces the need for refresher training on EID-DBS training.

No conflict of interest

Abstract: A_10

Prevention of Mother-to-Child transmission

Monitoring of infants HIV-positive mothers insolidarity social action center of Bouake-Cote d'Ivoire

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Introduction: According to UNAIDS, 330,000 children were infected with HIV in 2011, of which over 90% live in sub-Saharan Africa. The majority of pediatric AIDS cases resulting from the mother to child transmission of HIV.

Objective: Take stock of the prevention of mother- to- child HIV transmission effected Solidarity Social Action Center of Bouake in the perspective of reducing the incidence of pediatric HIV / AIDS.

Patients and methods: We performed a retrospective descriptive study referred to Solidarity Social Action Center of Bouake. It was to describe the epidemiological, clinical, biological and evolutionary infants of HIV positive mothers on ARV, born in the period 2009-2011. The parameters of the study were family history , circumstances of birth , methods of feeding , monitoring infant and evolutionary terms of infected infants. Analysis and data mining have been possible thanks to the software word, excel and epi info Version 7.

Results: Hundred and thirty two infants were selected in the study. Ninety (68%) mothers were receiving HAART during pregnancy and 111 (84%) gave birth in a health facility. Hundred seventeen (89%) children were born vaginally and 98 had good Apgar. The sex ratio was 0.76 and 115 (87%) infants received ARV prophylaxis at birth. The rate of mother to child transmission of HIV was 6.82%. Our rate was influenced by certain variables studied. Indeed, mothers who received ART before pregnancy had no children infected with HIV. Eighty percent of infected children were born to HIV-positive parents. All children born by caesarean section at the University Hospital and were not contaminated. Infants who received no postnatal prophylaxis ran more risk of being infected (p = 0, 0088, CI [2.50 to 29.78]). Mixed feeding also favored the mother-child transmission of HIV (p = 0.015, CI [1.99 to 25.62]).

Conclusion.: ARV treatment during pregnancy remains essential to reduce mother to child transmission of HIV. It will be more effective if it is coupled to the ARV prophylaxis at birth. This requires strict compliance with the recommendations of various national and international organizations.

No conflict of interest

Abstract: A_11

Prevention of Mother-to-Child transmission

Survival of HIV positive infants identified through the Haiti national Early Infant Diagnosis Program

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Introduction: The prime purpose of EID is to reduce the very high mortality rate of infants who are either born HIV positive or become infected early. Rapid identification of these children using dried blood spots from 4 weeks of age has allowed the Haitian program to promote the early initiation of ART that has been demonstrated to reduce mortality. The National Program started in 2009 and now covers over 100 hospitals providing national coverage of the population. The EID program follows up every child identified as positive at the sites using site visits and electronic medical records. We wanted to know how the program performed in its aim to start children on ARVs and to assess the survival of children identified.

Material & Methods: Using information sheets collected at the time of testing and our follow up systems we analyzed the number of children tested and the progress of HIV positive infants. Data is presented for all sites enrolled in the program except 2 where the data is unavailable.

Results: From 2011 to 2013 586 HIV positive children were identified from whom 143 (24%) died 78 (13%) were lost to follow up 365 (62%) were alive and 271 (46%) were on ART as of January 31,2014It is worth noting that there has been a decrease in mortality from 30% in 2011 to 10% in 2013 as well as a decrerase in lost to follow up from 15% in 2011 to 7% in 2013

Conclusions: Since 2011, the EID program has identified 586 HIV positive children.62% are still alive and 46% are on ARVs. However with an overall mortality of 24% and loss to follow up of 13% there is still much to be done to improve the survival of this vulnerable group

No conflict of interest

Abstract: A_12

Prevention of Mother-to-Child transmission

Challenges to Virtual Elimination of Mother to Child Transmission (eMTCT) at Mulago National Referral Hospital.

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Background: Uganda is aggressively pursuing virtual elimination of mother to child transmission (eMTCT) by 2015. This concept involves identification of HIV infection in women, and initiation of ART treatment as early as possible during pregnancy, through labor/delivery and the postpartum with ARVs for the rest of life, offering Nevirapine (NVP) syrup to all HIV exposed infants and infant feeding counseling among others. Even with these efforts in place, women still pass on HIV infection to their children.

Method: At Mulago National Referral Hospital post natal Clinic (PNC), all HIV exposed infants brought back at 6 weeks are offered Polymerase Chain Reaction (PCR) test. PMTCT program counselors interviewed mothers whose infants were found to be HIV positive after receiving the first PCR test to identify challenges that may be associated with acquiring HIV infection among their infants.

Results: Data analysis showed that 570 infants were tested from November 2013 – February 2014 and 14/570 (2.5%) had turned positive. Among the 14 women whose infants turned positive, 8/14 (57.1%) reported receiving antiretroviral drugs, 3/14 (21.4%) tested negative during pregnancy but sero converted later, 2/14 (14.2%) did not receive ARVs while 1/14 (7.1%) delayed receiving ARVs during pregnancy. Among the 14 infants who turned positive, 3/14 (21.4%) did not receive NVP syrup after delivery. The feeding options reported by the mothers included 1) exclusive breastfeeding, 10/14 (71.4%), 2) cow's milk, 2/14 (14.3%) and 3) mixed feeding 2/14 (14.3%). Other issues reported included poor adherence to ARVs which was reported by 21.4% of the 14 mothers

Conclusions: Common factors associated with HIV infection among infants identified included lack of receipt of ARVs for pregnant mothers and infants, poor ARV adherence, sero conversion and practice of mixed feeding. Developing counseling key messages to address the above issues will be crucial in elimination of mother to child transmission.

No conflict of interest

Abstract: A_13

Complications of HIV therapy

Use of efavirenz during the first trimester and resulting pregnancy outcome: Experience of the Ambulatory Treatment Center of Brazzaville

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Background: The aim of this study is to report the experience of the Ambulatory Treatment Center of Brazzaville regarding the use of efavirenz (EFV) during pregnancy.

Methods: A retrospective cohort study of HIV-positive women was conducted at the Ambulatory Treatment Center of Brazzaville. The study examined the use of an anti-retroviral treatment containing EFV in women who reported being pregnant during follow-up between January 2009 and September 2011. Demographic, clinical and biological data, and adverse effects associated with exposure to EFV during pregnancy were assessed after each pregnancy from the register of pregnant women in terms of preterm delivery (birth occurring before 37 weeks of age) and spontaneous miscarriage (spontaneous expulsion of the fetus before 15 weeks of age).

Results: Of 220 patients on an antiretroviral treatment who reported being pregnant during follow-up, 34 patients were administered combinations containing two nucleoside reverse transcriptase inhibitors (AZT/3TC=27; d4T/3T =4; TDF/FTC=3) and EFV, with a median age of 31.95 years (IQR: 27.71-36.37) and median durations of exposure to EFV of 11.81 months (IQR: 5.46-21.22) and 35.14 weeks (IQR: 11-39.86) before and during pregnancy, respectively. In 13 patients who reported to be in their first trimester of pregnancy, a change from EFV to nevirapine was made in nine of these patients. The median CD4 count was 271.5 cells/mm3 (IQR: 233.5-414.5) and 305 cells/mm3 (IQR: 205-408) in early pregnancy and at delivery, respectively; the viral load was undetectable in 90% and 85.7% of the patients, respectively. Twenty-three deliveries took place after 37 weeks gestation; additionally, adverse fetal outcome included: three infants born with low birth weight, five preterm deliveries, four spontaneous miscarriages, one terminated pregnancy, and one death in utero occurred. No infants were HIV-infected.

Conclusions: EFV used during the first trimester of pregnancy offers security, but the number of adverse fetal outcome is also important, among African women HIV-infected.

No conflict of interest

Abstract: A_14

Complications of HIV therapy

Lipodystrophy syndrome among HIV infected children on highly active antiretroviral therapy in northern India

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Introduction: it is estimated that about 2.5 million people are living with HIV infection in India. Although antiretroviral drugs have been able to reduce the mortality , these drugs have serious side effects one of which is lipodystrophy syndrome.Most of the drugs used in Highly Active Antiretroviral Therapy(HAART) viz, protease inhibitors, stavudine, and nevirapine are associated with lipodystrophy, hence we conducted this study to assess the prevalence of lipodystrophy in HIV infected children on HAART and its associated risk factors.

Materials and methods: a cross sectional study was conducted on 80 HIV infected children aged 2-18 yrs of age who were on stavudine based HAART for ≥ 2 years. These children were assessed for the presence of

lipodystrophy and its metabolic complications and associated risk factors.

Results: lipodystrophy was observed in 33.7% of children with lipoatrophy being the commonest subtype followed by lipohypertrophy. Older age, increased duration of treatment, and dyslipidaemia were found to be associated in patients with lipodystrophy than those without. On further multivariate analysis of independent risk factors only increased duration of treatment was significantly associated with lipodystrophy. no association was found with insulin resistance.
conclusion - we observed that lipodystrophy is a common finding in HIV patients treated with HAART for long duration.

No conflict of interest

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