PA-402 PREDICTORS OF ARCHIVED HIV-1 DRUG RESISTANCE MUTATIONS IN CELLULAR RESERVOIRS OF VIRALLY SUPPRESSED ADOLESCENTS: THE EDCTP READY-STUDY TMA2025-CDF1027

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Background Even though 92% of people receiving antiretroviral treatment (ART) have achieved viral suppression (VS) globally, adolescents with perinatal HIV-infection (APHI) have challenges in sustaining VS, probably due to HIV-1 archived drug resistance mutations (ADRMs). Our objective was to investigate on ADRMs among APHI on VS in Cameroon.
Methods An analytical study was conducted in 2021 among 38 consenting APHI on VS at the Chantal BIYA International Reference Centre (CIRCB) in Yaoundé-Cameroon. Proviral-HIV-1 DNA was extracted from buffy coat, DNA extracts were amplified, purified and sequenced by capillary electrophoresis. Generated proviral sequences were used to analyse ADRMs on HIVdb.v9.0. Molecular phylogeny was performed with MEGA v10x and data were analysed with a significance threshold of 5%.
Results A total of 30 samples were successfully amplified, of which 28 sequences were obtained and one sequence was excluded due to APOBEC3G mutations. Sex ratio M/F was 3/4; median age was 14 years [IQR: 13–16.5]. Regarding ART, twelve (42.9%) were on first line, and the most common regimens were TDF+3TC+EFV and TDF+3TC+ATV/r; and 64.3% (18/28) were fully adherent. Regarding ART response, 92.9% were at WHO clinical stages 1/2; median CD4 was 642 [IQR: 421–769] cells/mm3; 32.1% (09/28) had undetectable viraemia. The prevalence of ADRMs was 59.2% (16/27), of which main DRMs by class were M184MV/I (25%), T215Y/IL/FS (15.9%) for nucleoside reverse transcriptase inhibitors (NRTIs); K103K/N (25.7%), A98A/G (14.3%) for non-NRTIs; I54V and V82VA (3.7% each) for PI/r. Second line of ART were associated with ADRMs (p=0.001). ADRMs were found in detectable (66.6% i.e. 12/18) versus undetectable viraemia (44.4% i.e. 04/09), p=0.58. Seven HIV-1clades were found, with CRF02_AG being prevalent (67.8%).
Conclusion Despite VS, APHI harbour ADRMs, which underscore high risks of subsequent ART failure, even with undetectable viraemia. Limiting emerging ADRMs suggest targeting APHI on second-line ART, after previous exposure to NRTI-containing regimens.

PA-404 NEUTROPHIL ASSOCIATED MARKERS IN SPUTUM TO PREDICT POSTTB LUNG IMPAIRMENT

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Background Tuberculosis (TB) is the #1 bacterial killer worldwide. Despite of successful antibiotic treatment, exacerbated patients did not regain sufficient lung capacity and develop postTB lung disease (PTLD). We hypothesized, that neutrophils play an important role in disease exacerbation and associated marker can be used for early detection of PTLD.
Methods 25 confirmed MDR-TB Patients were recruited, sputum samples were taken over 6 months and analyzed for neutrophil associated proteins by ELISA. TB severity was assessed at baseline and month 6 using spirometry (lung function) and x-ray (lung pathology). Patients were categorized in mild and severe diseased by using Ralph score (threshold 40 pts) or spirometry (threshold FVC<0.85*LLN.FVC or gli.FEV1.zscore<-2).
Results 16 patients (64%) had a stable severe impairment in lung function and no improvement after 6 month was observed. In contrast, x-ray pathology was improving in 10 patients (40%) and remained stable severe in 10 patients (40%). Ralph scores were significantly higher in patients with impaired lung function. Neutrophil associated marker significantly declined under antibiotic treatment. Patients with stable severe impairment have significantly increased MMP8 sputum concentrations at baseline (p = 0.017) and increased concentrations of Calprotectin (p = 0.008), MPO (p = 0.034), ELA2 (p =0.031) and NGAL (p = 0.01) at week 2. In addition, Calprotectin (p = 0.005), MMP8 (p = 0.011) and NGAL (p = 0.03) concentrations were increased in males at month 4, while no sex differences in x-ray pathology was observed.
Conclusion Early postTB lung impairment was associated with neutrophil proteins in acute TB and elucidate the impact of neutrophils on disease progression and immune pathology. These proteins will be further analyzed as targets for Host Directed Therapies to reduce oxidative stress, tissue degradation, as well as immune modulators to prevent PTLD.

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PA-407 SUPPORTING WOMEN LEADERSHIP IN GLOBAL HEALTH RESEARCH

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Background According to WHO only 25% of women in the health workforce are in senior positions. Underrepresentation of women in leadership positions in biomedical research has contributed to gender bias in research questions, study designs,