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Examining Immune Markers as Determinants of Cognitive Difficulties Among Perinatally Infected Youth with HIV

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Introduction

- Perinatally acquired HIV (PHIV) remains a major global health challenge with an estimated 2.7 million youth affected worldwide. 90% of PHIV youth reside in low- and middle-income countries where access to antiretroviral therapy (ART) remains incomplete.
- PHIV youth experience cognitive difficulties when compared to uninfected peers, including deficits in:
  - Learning and memory
  - Processing speed
  - Executive function
  - Motor function
- PHIV youth who survive the early years of life with ART exhibit unique cognitive-immune profiles when compared to adults with chronic HIV.
- Elevated immune factors present in childhood may exacerbate adverse effects of HIV on these individuals as they progress into adolescence
- ***Research question:*** What is the relationship between immune markers and cognitive outcomes among PHIV youth compared to HIV- youth?

Methods

- Participants included 105 PHIV youth and 44 HIV- youth residing in two privately funded orphanages in Yangon, Myanmar. Each orphanage provided similar education, nutrition, recreational activities, and care.
- PHIV youth had confirmed serostatus and were taking ART for ≥ 24 months. PHIV youth maintained 100% adherence to ART regimen under daily supervision by the orphanage staff.
- Demographic and clinical data was collected through staff interview and medical record review. Blood was collected and assayed for immune markers per standard protocols.
- Cognitive testing was conducted by trained pediatricians. The battery consisted of culturally relevant measures of executive function, learning and memory, psychomotor and processing speed, visuospatial, and gross motor.
- Groups were compared using ANCOVAs (covarying for demographic/clinical differences), and Pearson correlations were used to compare cognition and immune biomarkers

Variable	PHIV (n=105)	HIV- (n=44)	*p* value
Age, M (SD)	12.88 (2.22)	13.95 (1.29)	**.003**
Sex (% male)	52 (50.0%)	17 (38.6)	.205
Number of Months Residing in Orphanage, M (SD)	82.85 (33.76)	63.70 (27.85)	**.001**
Grade, M (SD)	5.19 (2.32)	7.11 (1.47)	**<.001**
Current CD4+ T-cell count, Median (IQR)	729 (565-1026)	798 (690-905)	.753
HIV Viral Load, n (%) undetectable	85 (81.7%)	-	-
CD14 Count (log10), Median (IQR)	6.24 (6.15-6.32)	6.05 (5.99-6.11)	**<.001**
CD163 Count (log10), Median (IQR)	5.14 (4.89-5.34)	4.83 (4.65-5.04)	**.027**

Fig. 1 Demographic and Clinical Characteristics of HIV positive and negative youth

Test	PHIV (n=105)		HIV- (n=44)	
	CD14	CD163	CD14	CD163
Color Trails 2	.173	.065	-.083	-.049
Digit Span Forward	-.060	-.162	-.003	.085
Digit Span Backward	**-.199***	-.187	-.027	-.142
Animal Fluency	-.146	**-.201***	.136	.037
Food Fluency	-.077	-.113	.118	-.184
HVLT-R Total Learning	-.055	-.174	.048	**-.350***
BVMT-R Total Learning	-.021	-.056	.143	-.112
HVLT-R Delayed Recall	-.076	-.102	.171	-.183
BVMT-R Delayed Recall	-.017	-.027	.174	-.010
Grooved Pegboard-Dominant	-.033	.176	.075	-.063
Grooved Pegboard-Nondominant	.000	.121	.128	.042
Color Trails 1	-.014	.184	.030	.137
Trails A	-.037	.075	**.353***	-.056
Digit Symbol	-.142	-.108	-.202	-.105
Symbol Search	-.129	-.195	-.003	-.134
Block Design	-.030	-.126	-.128	-.175
Beery VMI	-.023	-.196	.055	.005
Timed Gait	**.314****	-.031	.051	-.041

** $p < .01$; * $p < .05$

Fig. 2 Correlation between raw cognitive test scores and immune markers in HIV positive and negative youth

Results

- PHIV individuals were younger, were in a lower grade, and had spent a longer time residing in the orphanage than individuals without HIV
- PHIV performed worse than youth without HIV on all cognitive domains
- Among PHIV, greater levels of immune biomarkers were associated with poorer cognitive performance on measures of Executive Function and Gross Motor
- Worse performance on measures of Learning and Psychomotor/Processing Speed were correlated with higher immune biomarkers among individuals without HIV

Discussion

- Children with HIV exhibited poorer neurocognitive function in all domains than youth without HIV
- Higher inflammatory markers, including CD14 and CD163, correlated with worse neurocognitive function in PHIV children
- Elevated immune biomarkers present during the transition to adolescence may exacerbate the effect of HIV on neurocognition
- HIV+ children from resource-limited countries face challenges such as malnutrition, poor education, and family stress, which may contribute to cognitive difficulties
- Protective factors such as higher household income and social support contribute to resilience in PHIV children
- Understanding the interactions and synergistic effects of peripheral markers of immune activation can aid in earlier diagnosis, accurate prognosis, and effective treatment of neurocognitive decline among PHIV