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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

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