Vascular Health and Cerebral Blood Flow in Perinatally HIV-Infected Children

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Higher CRP levels and lower grey matter perfusion were associated with white matter injury, and higher sVCAM-1 with poorer visuomotor integration.

These results suggest that vascular disease may play a role in cerebral injury and cognitive impairment in pediatric HIV.

KEY POINTS:
- Perinatally HIV-infected children showed higher plasma CRP and sVCAM-1 levels, and higher subcortical and white matter cerebral blood flow as compared to controls.
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VASCULAR MARKERS IN PLASMA AND CSF

HIV-infected children showed higher systemic levels of CRP and sVCAM-1, as well as higher concordance between blood and CSF levels of CRP and sVCAM-1 (Table 2).

CONCLUSIONS
In a well-treated cohort of perinatally HIV-infected children, ongoing inflammation and endothelial activation were indicated by elevated systemic CRP and sVCAM-1, which showed strong concordance with CSF levels. Further, they had higher CBF in white matter basal ganglia and thalamus, potentially indicating increased metabolic demand or low-grade inflammation in these brain regions.

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BACKGROUND
Despite effective virological suppression with cART, children perinatally infected with HIV show neurodevelopmental dysfunction, possibly due to micro- and macrostructural brain injury. Chronic pediatric HIV infection and several components of cART have been associated with vasculopathy, coagulopathy, metabolic comorbidities, and an increased risk of cerebrovascular events. However, the interplay between these factors and cerebral perfusion, structure and function is unknown.

This study aimed to assess vascular disease biomarkers and cerebral blood flow (CBF) in HIV-infected children, and to explore potential associations with cerebral and cognitive deficits.

METHODS
This cross-sectional study included 36 HIV-infected children and 37 uninfected controls (Table 1). The large majority of HIV-infected children were virologically suppressed on cART at time of inclusion.

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RESULTS
CBF was determined using arterial spin labeling on a 3-Tesla MRI (Figure 1). MesoScale Discovery, and coagulation (using enzyme-linked immunosorbent assays) were measured in blood samples from all participants and in cerebrospinal fluid (CSF) from HIV-infected participants. CBF was determined using arterial spin labeling on a 3-Tesla MRI (Figure 1).

Figure 1. Arterial spin labeling to measure regional cerebral blood flow.

Figure 2. Figure 2. Cerebral blood flow, measured using arterial spin labeling on a 3-Tesla MRI (Figure 1).

Figure 3. Correlations of inflammatory and endothelial activation markers with cerebral injury and cognition dysfunction. A higher CRP was associated with increased cerebral blood flow, indicating increased metabolic demand or low-grade inflammation in these brain regions.

Figure 4. HIV-infected children have higher cerebral blood flow in white matter, basal ganglia and thalamus. Data was available for 35 included children and 36 controls; exclusions were due to motion or labeling artefacts or lack of T1 contrast. We compared CBF between groups using Mann-Whitney-U test adjusted for age, corrected for sex and corrected for age. The baseline subject-wise CBF maps were generated using an arterial spin labeling protocol with an overall mean gray matter CBF. Lower gray matter CBF and elevated inflammation (CRP) were associated with white matter injury, and lower sVCAM-1 with poorer visuomotor integration. Vascular disease may thus play a role in pediatric HIV-associated cerebrovascular and cognitive deficits. Longitudinal evaluation is warranted to assess whether CBF changes, inflammation, and endothelial activation negatively affect white matter health and cognitive performance in this population over time.