

The association of systemic inflammation and cognitive functions of pre-school aged children residing in a *Schistosoma haematobium* endemic area in Zimbabwe

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Abstract

Background: Cognitive function is negatively impacted by schistosomiasis and might be caused by systemic inflammation which has been hypothesized to be one of the mechanisms driving cognitive decline. This study explored the association of systemic inflammatory biomarkers; interleukin (IL)-10, IL-6, IL-17, transforming growth factor (TGF- β), tumor necrosis factor (TNF- α), C-reactive protein (CRP) and hematological parameters with cognitive performance of preschool-aged children (PSAC) from an *Schistosoma haematobium* endemic area.

Methods: The Griffith III tool was used to measure the cognitive performance of 136 PSAC. Whole blood and sera were collected and used to quantify levels of IL-10, TNF- α , IL-6, TGF- β , IL-17 A and CRP using the enzyme-linked immunosorbent assay and hematological parameters using the hematology analyzer. Spearman correlation analysis was used to determine the relationship between each inflammatory biomarker and cognitive performance. Multivariate logistic regression analysis was used to determine whether systemic inflammation due to *S. haematobium* infection affected cognitive performance in PSAC.

Results: Higher levels of TNF- α and IL-6, were correlated with lower performance in the Foundations of Learning domain ($r = -0.30$; $p < 0.001$ and $r = -0.26$; $p < 0.001$), respectively. Low cognitive performance in the Eye-Hand-Coordination Domain was observed in PSAC with high levels of the following inflammatory biomarkers that showed negative correlations to performance; TNF- α ($r = -0.26$; $p < 0.001$), IL-6 ($r = -0.29$; $p < 0.001$), IL-10 ($r = -0.18$; $p < 0.04$), WBC ($r = -0.29$; $p < 0.001$), neutrophils ($r = -0.21$; $p = 0.01$) and lymphocytes ($r = -0.25$; $p = 0.003$) The General Development Domain correlated with TNF- α ($r = -0.28$; $p < 0.001$) and IL-6 ($r = -0.30$; $p < 0.001$). TGF- β , L-17A and MXD had no significant correlations to performance in any of the cognitive domains. The overall general development of PSAC was negatively impacted by *S. haematobium* infections (OR = 7.6; $p = 0.008$) and (OR = 5.6; $p = 0.03$) where the PSAC had higher levels of TNF- α and IL-6 respectively.

Conclusion: Systemic inflammation and *S. haematobium* infections are negatively associated with cognitive function. We recommend the inclusion of PSAC into mass drug treatment programs.

Keywords: Cognitive functions; Cytokines; Hematological parameters; Pre-school aged children; Schistosomiasis; Systemic inflammation.