ABSTRACT

Reduced plasma levels of GM-CSF as biomarker of *Schistosoma mansoni* infection in school aged children

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Schistosomiasis is a neglected tropical disease (NTD) that persists despite decades of intensive global control efforts. Diagnosis in low burden settings and logistically easy to use morbidity monitoring tools are lacking and much needed to facilitate the elimination of the disease as a public health problem by 2030. Since, the infection associates with a highly dynamic host cytokine response, we comprehensively evaluated the potential of host plasma cytokines as biomarkers of intestinal Schistosomiasis and/or associated liver fibrosis. We performed a cross-sectional study on school children from a *Schistosoma mansoni* endemic area in rural Cameroon. Participants were screened for schistosomiasis and liver fibrosis using Kato Katz and ultrasonography, respectively. Plasma cytokines were screened and compared between phenotypical distinct groups (harbouring or not infection or morbidity) by Luminex in a discovery set of samples; identified candidate cytokines of dissimilar plasmatic levels were further confirmed by ELISA on a validation set of samples. Data were compiled in Excel software, analysed with RStudio and graphs plotted with GraphPad Prism.From a preliminary screening of 27 plasma cytokines by Luminex on the discovery set of participants, only three candidate cytokines were altered by the host infectious or pathology profile i.e. GM-CSF, IL-2 and VEGF. Cytokine-specific ELISA assays on a separate set of validation participants confirmed children with *S. mansoni* infection to present with significant lower plasma levels of GM-CSF and IL-2 when compared to *S. mansoni*-negative children. Further assessment of the biomarking potential of these cytokines revealed a positive correlation between plasma levels

of GM CSF, but not those of IL-2, and *S. mansoni* egg burdens in infected individuals. Moreover, when applying a threshold of plasma GMCSF levels for the screening of *S. mansoni* at-risk children , we could achieve an augmentation of the sensitivity of a single Kato-katz by at least 20%. Finally, a Receiver operating Characteristic Curve of GM-CSF performance as a predictive marker of *S. mansoni* infection in our study population yielded an Area Under the Curve of 75%, confirming the possible use of plasmatic levels of GM-CSF as good predictive marker of *S. mansoni* infection. In conclusion, our work revealed the potential of biomarking *S. mansoni* infection by comparative measurements of plasma GM-CSF. A basis for the refined use of plasma GM-CSF as a Schistosomiasis adjunct diagnostic tool is herein suggested.