Title: Association of current intestinal schistosome infection status with periportal fibrosis: a systematic review and meta-analysis

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Background: Periportal fibrosis (PPF) is a severe morbidity caused by exposure to intestinal schistosome infections. In the context of repeated mass drug administration, it is unknown whether PPF correlates with schistosome infection. We aimed to assess the association between current infection status and intensity of *S. mansoni, S. japonicum,* or *S. mekongi* and periportal fibrosis.

Methods: In this systematic review and meta-analysis, we searched the Cochrane Central Register of Controlled Trials, Embase, Global Health, Global Index Medicus and Medline on May 18, 2022, for studies of original research. Only studies that actively diagnosed current schistosome infection at the time of PPF measurement were included and underwent a risk of bias assessment. A meta-analysis of data extracted from published reports was conducted when the findings of more than three studies could be combined. Pooled effect sizes for binary PPF outcomes against current schistosome infection status were calculated using inverse-variance weighted random effects meta-analysis. The protocol was prospectively registered 19th May 2022 with PROSPERO (CRD42022333919).

Findings: We identified 2646 references; 37 were included in the systematic review and 30 were used to calculated pooled effect sizes across 17784 participants. PPF was heterogeneously defined with the Niamey protocol most often used to guide ultrasound assessments. Individuals with any current schistosome infection were 2·5 (95% CI:1·71-3·66) times more likely to have PPF but heterogeneity was high (I^2 statistic 94·8%). This association was not observed in studies with a low risk of bias. Subgroup analyses reduced heterogeneity within ultrasound protocol, study setting, PPF outcome, ultrasound pattern classification, study continent, study design and high risk of bias studies. No significant association was found between a secondary outcome of schistosome infection intensity and PPF status.

Interpretation: Guidelines use current schistosome infection as a proxy for PPF morbidity. This study supports that current infection status but not intensity is associated with an increased likelihood of having PPF. Current associations of infection status with PPF had limitations regarding the lack of adjusting for confounders, limited sample sizes, and loss of association in studies conducted after widespread mass drug administration. Further work is needed to identify associations of current infection status with different severity stages of PPF to effectively develop guidelines for morbidity.