

VOLUME 101

NOVEMBER 2019

NUMBER 5 SUPPLEMENT

SIXTY-EIGHTH

ANNUAL MEETING

November 20–24, 2019 │ astmh.org │ ajtmh.org │ **>**#TropMed19 #lamTropMed

GAYLORD NATIONAL RESORT AND CONVENTION CENTER NATIONAL HARBOR, MARYLAND, USA

Supplement to

The American Journal of Tropical Medicine and Hygiene



AN UPDATE ON THE ROLE OF IMAGING IN THE CARE OF PATIENTS WITH SCHISTOSOMIASIS

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Schistosomiasis leads to significant morbidity and mortality worldwide. Infection with Schistosoma mansoni and S. japonicum can lead to severe hepatic disease including periportal liver fibrosis and portal hypertension. Previous studies recommend the use of abdominal imaging to detect early hepatic changes and improve disease outcome. However, there are no recently published or authoritative resources to guide the use of imaging in the initial diagnosis of schistosomiasis. We searched available literature regarding the role of imaging in the evaluation of patients with schistosomiasis and aim to synthesize clinical recommendations. Eight electronic databases were searched: Ovid Medline, EMBASE, Cochrane Library of Systematic Reviews, Epistemonikos, Global Health, NICE, TRIP and LILACS with the following search terms: [Schistosomiasis OR (Schisto* AND (mansoni OR japonicum))] AND [CT OR (computed AND tomography) OR Ultraso* OR Sonogr* OR MRI OR (Magnetic AND resonance AND Imaging) OR Echo OR Imaging] AND [Liver OR periportal OR peri-portal OR fibrosis OR hepat* OR echogenic* OR (portal AND hypertension)] from database inception to February 28, 2019. A total of 2977 articles were identified: 691 articles on Ovid Medline, 30 Cochrane, 1035 Embase, 10 Epistemonikos, 516 Global Health, 34 NICE, 529 TRIP, and 132 LILACS. A total of 1933 articles remained for title screening after de-duplication. Titles, abstracts and full-texts were systematically double-screened by two reviewers and a tertiary arbitrator. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was employed. Two reviewers performed data extraction and quality of the studies was assessed with the Grading of Recommendations Assessment, Development and Evaluation (GRADE). Data were summarized using qualitative and quantitative measures to evaluate the role of imaging in the clinical management of schistosomiasis. Synthesizing the current literature on abdominal imaging in the evaluation of schistosomiasis can translate into clinical recommendations for improved risk stratification and overall management of schistosomiasis.

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SCHISTODETECT™: DEVELOPMENT OF A RELIABLE AND SENSITIVE RAPID DIAGNOSTIC TEST FOR SCHISTOSOMA JAPONICUM INFECTION IN HUMANS

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Zoonotic schistosomiasis continues to be a public health problem in Asian countries including China, the Philippines and Indonesia. Improving the diagnostic tools for surveillance in areas which have reached elimination level will help hasten the possible elimination of this disease. There is a critical need therefore for a rapid, low cost and highly sensitive point-of-care test (POCT) for the detection of specific antibodies in individuals infected with *Schistosoma japonicum*. For the development of the POCT,

several schistosome proteins were screened for their antigenicity using different serum panels (negative non-endemic and endemic samples, microscopy/PCR positive samples). ELISA results showed that 5 antigens, thioredoxin peroxidase SjTPx-1, phytochelatin synthase SjPCS, major egg protein fragment Sjp40M tandem repeats Sj7 and Sj11, provided above 70% detection rate. SjTPx-1 and Sj7 showed the highest sensitivity and specificity. Analyses on responses of schistosome-infected individuals to these antigens suggested that SjTPx-1, the best antigen, can be complemented by other antigens for better diagnostic performance. Out of these antigens, 6 fusion proteins were constructed and produced for serological evaluation. ELISA results showed that SjTP7 (SjTPx-1, SjPCS and Sj7 fusion) and SjT47 (SjTPx-1, Sjp40M and Sj7 fusion) have the highest diagnostic potentials among the fusion proteins. However, as compared to the single antigens, SjTPx-1 remained to be the best antigen for the diagnosis of human schistosomiasis. Optimization of different formats of the rapid test kit was done using sera obtained from screening in an endemic municipality in the Philippines. It was concluded that the best working format for the rapid test involves SjTPx-1 antigen. Overall, it was concluded that SjTPx-1 alone is not effective in rendering the rapid test sensitive. Future efforts should focus on generating recombinant fusion proteins with improved yields and robust performance in the rapid test format.

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DEVELOPMENT OF A SENSITIVE, QUANTITATIVE PCR ASSAY FOR THE DETECTION OF SCHISTOSOMA MANSONI TO AUGMENT STOOL SURVEYS FOR STH

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Schistosomiasis is a neglected tropical disease (NTD) that affects more than 200 million people globally. The causative agents of this infection in humans are the parasitic nematodes Schistosoma mansoni, Schistosoma haematobium and Schistosoma japonicum. Among other factors, the success of MDA relies on good diagnostic tests to identify endemic regions and to monitor the progress of MDA campaigns. Since we have already developed a series of qPCR tests that are exquisitely sensitive and species-specific for all of the soil-transmitted helminth (STH) parasites using a novel bioinformatics pipeline, it was logical for us to use the same approach to develop a quantitative, real-time PCR diagnostic assay for S. mansoni to add to our STH battery of tests for use in the largescale stool surveys in which we participate. This bioinformatics pipeline uses a novel tool, RepeatExplorer, to identify highly repetitive DNA elements in the genome of any eukaryote. We have already used this approach to successfully develop qPCR assays for Necator americanus, Ancylostoma duodenale, Ancylostoma ceylanicum, Trichuris trichiura, Ascaris lumbricoides and others. The same method was applied to both S. mansoni and S. haematobium to design primers and probes to target these important parasites. Using DNA isolated from S. mansoni and S. haematobium specimens obtained from the Natural History Museum (London, UK), two new qPCR tests were designed and optimized. In addition to testing the assays on purified DNA, a spiking study was also performed to demonstrate the sensitivity and specificity of the assays on human stool samples with S.mansoni and S. haematobium eggs added in various concentrations. Next steps include a field study in Uganda to assess the use of these assays in parallel with our existing STH tests.