A Systematic Review of the Risk of HIV Transmission with Concurrent Schistosomiasis Infection

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Abstract

Schistosomiasis and HIV are both significant causes of morbidity in low resource settings worldwide, particularly in Sub-Saharan Africa. Research has indicated that there may be a link between the two infections--specifically that schistosomiasis infection may be a risk factor for HIV transmission. A systematic review with meta-analysis exploring the interaction of the two infections was conducted to analyze this relationship. An exhaustive search in Pubmed and Google Scholar of was conducted with search terms related to schistosomiasis and HIV, and studies that were published within the past 30 years in English were included. In total, eight studies with similar outcome measures were found. Odds ratios of HIV transmission in patients with schistosomiasis infection were extracted and pooled. Pooled analysis of odds ratios extracted from the studies failed to find a statistically significant correlation between schistosomiasis infection and HIV infection. The pooled OR was 1.08 with a 95% confidence interval 0.81-1.35 and a p value of 0.056. These findings may indicate that there is not a relationship between the two infections, or they may be a result of the methods chosen for the meta-analysis. Notably, both S. mansoni and S. haematobium were included in the analysis, and it is possible that only S. haematobium significantly impacts HIV transmission. While the study did not result in significant findings, further research is warranted because of the public health implications if schistosomiasis is in fact a risk factor for HIV. This would suggest the possibility of HIV control via community-wide schistosomiasis treatment, a much more feasible and cost-effective intervention than expensive HIV medications.

Background

Schistosomiasis is a water-borne parasitic disease that causes significant morbidity worldwide with more than 260 million people affected worldwide in tropical regions spanning the globe, particularly sub-Saharan Africa. HIV/AIDS continues to be a major global public health issue, even with enormous improvements in treatment, causing the death of 1.5 million people in 2013 alone. Sub-Saharan Africa bears most of the burden of HIV with approximately 70% of both existing and new cases occurring in the region. Because of the regional overlap of the diseases, there has been extensive research into the relationship between the two infections. Several studies have indicated that there may be an increased risk of HIV transmission in patients with schistosomiasis infections.

Proposed theories for the mechanisms behind this increased risk include the following: First, the genital lesions present in urogenital schistosomiasis infections create entry points for the HIV virus. Second, there is increased recruitment of CD4 cells at the site of these lesions, creating additional targets for the HIV virus to infect. Third, the parasitic infection of schistosomiasis results in an increased Th2 immune response, lowering the Th1 immune response required to defend against the HIV virus.

Research Significance

An increased risk of HIV transmission in patients with schistosomiasis would have significant public health implications. Schistosomiasis is relatively inexpensive and simple to treat with a short course of antiparasitics while HIV continues to be incurable and requires expensive treatments to manage. A causal relationship between the two infections could mean that treating schistosomiasis infections may decrease the incidence of HIV.

Prior to this systematic review no recent reviews used an unbiased statistical analysis to examine the interplay between schistosomiasis and HIV. The most recent systematic review of the subject was published in 2011, and the numerous articles published since then suggested the need for a more updated review.

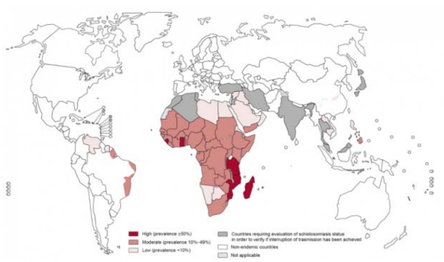

Figure 1: Global schistosomiasis prevalence in 2011

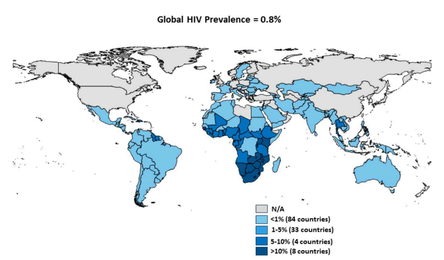

Figure 2: Global HIV prevalence in 2016

Methods

An exhaustive search for articles using PUBMED and Google Scholar was conducted with multiple search terms related to schistosomiasis and HIV. The search results were refined by language then primary research articles within the past 30 years were be selected. Case studies and articles written in a language over than English were eliminated. Eight studies were determined to meet the above criteria and include the appropriate measures. Odds ratios for infection with HIV in those with schistosomiasis infection were extracted from these studies. A pooled analysis of the ORs was conducted with the assistance of the statistics department.

Results

Pooled analysis of odds ratios extracted from the studies failed to find a statistically significant correlation between schistosomiasis infection and HIV infection. The pooled OR was 1.08 with a 95% confidence interval 0.81-1.35 and a p value of 0.056.

Author and Title	Year	Summary of Study
Downs, et al. *Urogenital Schistosomiasis in Women of Reproductive Age in Tanzania's Lake Victoria Region*	2011	457 women ages 18-50 from rural Tanzania. Tested for schistosomal infection by urine and genital ova. There was a significantly higher rate of HIV in women with schistosomiasis.
Downs, et al. *Association of Schistosomiasis and HIV Infection in Tanzania*	2012	345 women ages 15-50 from fishing villages in Tanzania where S. Mansoni is common. Tested for schistosomal infection by serum antigens. Schistosomiasis significantly predicted HIV infection.
Kjetland, et al. *Association between genital schistosomiasis and HIV in rural Zimbabwean women*	2006	527 sexually active, nonpregnant women ages 20-49 from rural Zimbabwe. Tested for schistosomal infection by urine or genital ova. Women with schistosomiasis were determined to have higher risk of being infected with HIV.
Mazingo, et al. *Co-infection with Schistosoma mansoni and Human Immunodeficiency Virus-1 (HIV-1) among residents of fishing villages of north-western Tanzania*	2014	1,785 adults aged 21-55 in fishing villages in Tanzania. Tested for schistosomal infection by stool ova. There was no association between schistosomal and HIV infections, including when stratified by intensity of infection.
Ndhlovu, et al. *Prevalence of urinary schistosomiasis and HIV in females living in a rural community of Zimbabwe: does age matter?*	2007	544 women aged 15-49 from rural Zimbabwe. Tested for schistosomal infection by urine ova. No significant association was shown between the infections in total but there was a significantly higher rate of HIV in women with schistosomiasis over age 35.
Sanya, et al. *Schistosoma mansoni and HIV infection in a Ugandan population with high HIV and helminth prevalence*	2015	1,412 adults over the age of 13 in a fishing village in Uganda. Tested for schistosomal infection by stool ova. Schistosomiasis was not found to be associated with HIV infection.
Kallestrup, et al. *Schistosomiasis and HIV-1 Infection in Rural Zimbabwe: Implications of Coinfection for Excretion of Eggs*	2005	1,545 adults over the age of 18 from rural Zimbabwe. Tested for schistosomal infection by urine and stool ova. There was no significant association found between the two infections.
Ssetala, et al. *Schistosoma mansoni and HIV acquisition in fishing communities of Lake Victoria, Uganda: a nested case control study*	2015	200 adults ages 13-49 from a fishing village in Uganda where S. mansoni infection is common. Tested for schistosomal infections by serum antigens. No significant infection was found between schistosomal and HIV infections.

Table 1: Studies selected for analysis

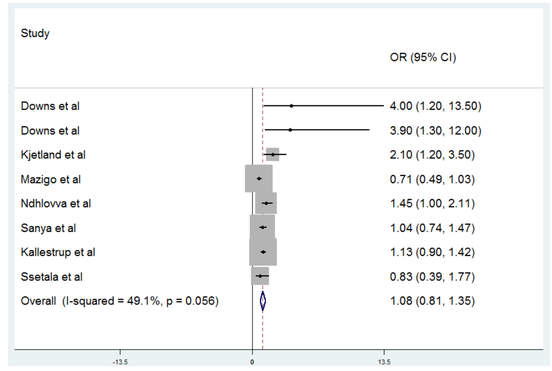

Table 2: Pooled odds ratios of HIV infection in patients with schistosomiasis infection from the relevant studies.

Discussion and Conclusions

The meta-analysis did not find a statistically significant increased risk of HIV infection in those with schistosomiasis infection. It is possible that this indicates that there is no relationship between the two infections, but it may also be because of the methods used in this study. This systematic review included studies with both S. haematobium and S. mansoni, and it is possible that only S. haematobium is associated with increased risk of HIV infection. This would be consistent with the proposed pathophysiology discussed prior, as it is primarily S. haematobium infections that cause mucosal damage that could be an entry point for HIV infection.

While the systematic review with meta-analysis did not result in a statically significant association between schistosomiasis and HIV, there were enough statistically significant studies to suggest that there may be a connection between the two infections. Additional research is needed to clarify this connection and the direction of causality. If schistosomal infections increase the risk of HIV transmission, it is possible that schistosomiasis treatment with antiparasitics would decrease HIV transmission.

Additional research is also needed to explore whether treating schistosomiasis could curtail the spread of HIV. If campaigns to treat schistosomiasis did decrease HIV transmission, new HIV infections and the resulting cost in both lives and dollars could be prevented with a relatively cheap and simple intervention. At this time, however, there is not enough evidence to suggest that such a strategy would be successful.

Acknowledgements

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