Invited Review

The soil-transmitted helminths in Sri Lanka: a review of the recent literature

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Abstract

The major soil-transmitted helminth (STH) infections caused by *Ascaris lumbricoides*, *Trichuris trichiura* and *Necator americanus* have been recognized as endemic in Sri Lanka for over a century. Although prevalence rates have declined drastically over this period because of mass deworming programmes and improved housing, these infections are still found in high risk communities with poor access to sanitation. The available scientific literature published on STH infections in Sri Lanka from around the year 2000 onwards is reviewed here in three broad areas: prevalence of STH infections and factors affecting transmission, impact of control activities on prevalence and drug resistance, and the impact of STH infections on the health of infected individuals. In conclusion, an overview of the current control strategy adopted by the Ministry of Health in Sri Lanka is presented.

Keywords: Soil-transmitted helminths, Ascariasis, Trichuriasis, Hookworm, Epidemiology, Morbidity, Control strategies

Introduction

The soil-transmitted helminths are among the most common parasites of humans.[1] The aetiological agents include the common roundworm (*Ascaris lumbricoides*), the whipworm (*Trichuris trichiura),* the hookworms (*Necator americanus* and *Ancylostoma duodenale*), and the threadworm (*Strongyloides stercoralis*), all of which are primarily parasites of humans. They are known as soil-transmitted helminths (STH) because their continued transmission is dependent on contamination of soil with the microscopic eggs or larvae of these helminths, as a result of open defaecation.

Ascariasis, trichuriasis and hookworm infections (the major STH infections) have been identified by the World Health Organization as common and important causes of morbidity among children. It is estimated that worldwide in 2010, approximately 820 million persons were infected with *A. lumbricoides*, 460 million with *T. trichiura*, and 440 million with *A. duodenale* or *N. Americanus*.[2]

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Infections are known to result in a range of clinical manifestations including malnutrition, intestinal and biliary obstruction, dysentery and anaemia. The highest prevalence occurs in areas where sanitation is inadequate and water supplies are unsafe. The strategy recommended by WHO to control morbidity from STH involves the periodic administration of anthelmintic medicines to populations at risk of disease, which includes pre-school age children, school age children and women of reproductive age.[3]

New infections of *A. lumbricoides* and *T. trichiura* are acquired by ingestion of eggs containing infective larvae, via direct ingestion of contaminated soil, or fruits and vegetables contaminated with infected soil. Infection with the hookworms occurs when the free-living larvae, which are found on the surface of contaminated soil, penetrate bare skin.

As a developing country with a warm, wet, tropical climate, Sri Lanka is also endemic for all three types of STH (excluding *A duodenale*). Hookworm infections were first identified in this country over one hundred years ago, in the late 19th century.[4] The public health impact of all three STH infections was well recognized[5-11] and extensive de-worming programmes were conducted over much of the 20th century. As a result of these programmes, combined with gradual improvements in housing and sanitation, as well as general health literacy, prevalence rates have drifted down steadily, albeit slowly. STH infections have, however remained endemic in Sri Lanka, and there is a significant body of work that has been published over the years, summarized by de Silva in 2005.[12]

This review summarizes the available scientific literature published on STH infections in Sri Lanka, from around the year 2000 onwards. The review is organized into three broad areas: prevalence of STH infections and factors affecting transmission; impact of control activities on prevalence and drug resistance; and the impact of STH infections on the health of infected individuals. In conclusion, an overview of the current control strategy adopted by the Ministry of Health in Sri Lanka is presented.

Prevalence of STH infections and factors affecting transmission

A nationwide survey of the health 9 – 10 year old school children, carried out in 2003, included examination for STH infections.[13] A total of 2,173 children from all nine provinces were examined using a single Kato-Katz smear of faecal samples. The cumulative prevalence (percentage of children with any STH infection) was estimated to be 6.9% among those examined. Whipworm was the most prevalent infection (4.0%), followed by roundworm (2.8%) and hookworm (1.2%). Cumulative prevalence was highest in the Eastern (12.3%), Northern (11.1%) and Western provinces (10.0%).

Other studies which have examined prevalence in more restricted populations around the same time include a survey of 743 schoolchildren attending Grades 1 – 5 in four schools in the Moneragala District in 1997.[14] Fresh stool samples were examined using the Kato-Katz methods. The prevalence of ascariasis, trichuriasis and hookworm infections were 2.0%, 0.7% and 5% respectively. In 2016, a survey of children attending 9 schools in the Kaduwela area which had been severely affected by floods, found that none of the 156 faecal samples examined by normal saline smears were positive for STH eggs.[15]

A detailed study conducted in the estate sector, which remains a high-risk community for STH infections in Sri Lanka, has examined in depth, factors that affect the prevalence of STH infections, to facilitate greater effectiveness in control activities. Different aspects of this study have been presented in sequential papers.

The first paper examines the relationships between the prevalence and intensity of human infection with *Ascaris* and the availability of sanitary facilities, socio-economic status and personal health habits.[16] During the period July – December 2000, 176 subjects, who lived on a low-country tea plantation, were investigated using Kato-Katz smears. Half (50.0%) of the subjects were found to be excreting *Ascaris* eggs. Almost all (96.6%) of the subjects lived in terraces of one-room houses built by the plantation owners, and only 30.7% had access to a latrine. Most (90.3%) obtained their drinking water from common taps, and 48.8% boiled their drinking water. The subjects who only drank water that had been boiled and those who washed their hands before meals were relatively unlikely to be infected. The authors concluded that even in congested living conditions with poor sanitary facilities, good hygiene and the boiling of all drinking water can reduce the risks of *Ascaris* infection.

The second paper examines the effect of seasonal variations in climatic conditions on transmission of *Ascaris* infections in two selected low-country plantations, during the period March 2000 – June 2001.[17] Faecal samples from 477 persons aged between 2 and 74 years were tested using the Kato-Katz method and the prevalence and intensity of infection determined. Monthly follow-ups were undertaken with similar stool examinations and treatment given with a single dose of mebendazole, if found positive. Infection and re-infection rates were calculated each month. Rainfall and temperature were recorded each day. Total rainfall, number of wet-days and mean temperature was calculated for each month. The prevalence of *Ascaris* infection was 53.4% and 51.0% at Maliboda and Ayr estates respectively. Highest infection and re-infection rates at Maliboda (37.7%, 37.2%) occurred in June and at Ayr (13.3%, 25.9%) in October 2000 respectively. During the study period, the mean rainfall was 28.1 cm (range 7.4-63.9 cm) and mean temperature 27.6 degrees C (range 22.1 degrees -34.4 degrees C). Significant correlations were found between the re-infection rate and rainfall, temperature and the number of wet-days. Similar correlations were observed with the infection rate and temperature and the number of wet-days. *Ascaris* infections were found to correlate significantly only with the number of wet-days in a month. The authors concluded that the number of wet-days appeared to be a better indicator of *Ascaris* infections than total rainfall or mean temperature.

The third paper examines the climatic, socio-economic and behavioural factors influencing *N americanus* infection in the same study population.[18] The baseline prevalence of hookworm infection was 28.5%, while the intensity of infection ranged from 0-4,828.5 eggs/g faeces, with a mean of 128.4 eggs/g. The monthly incidence of hookworm infection was found to show three peaks at Maliboda (September 2000 (21.3%), January 2001 (20.8%) and May 2001 (17.5%)), while two peaks were seen at Ayr (September 2000 (25.0%) and February 2001 (29.2%)). The authors found that the incidence of hookworm infection showed statistically significant correlation with mean temperature. Bathing and washing with water from rock-pools formed by waterfalls, the use of wells, and a lack of toilets were also found to increase the risk of hookworm infection significantly.

Some years later, data from these three studies were re-analysed to evaluate patterns of co-infection and changes in egg deposition.[19] This analysis found positive associations between *T. trichiura* and both *N. americanus* and *A. lumbricoides*, but no association between *N. americanus* and *Ascaris*. It was shown that *N. americanus* and *Ascaris* infections had lower egg depositions when they were in single infections than when they were co-infecting. There was no clear evidence, however, of a similar effect of co-infection in *Trichuris* egg deposition. The authors concluded that associations in prevalence and egg deposition in STH species may vary, possibly indicating that effects of co-infection are species dependent.

In a separate, cross sectional study conducted in 2013, 258 children aged 1 - 6 years, living on Uduwela tea plantation in the Kandy District were examined to determine the prevalence of ascariasis and factors associated with it.[20] Data regarding socio-demographic and hygienic habits were collected from heads of households via an interviewer administered structured questionnaire. Wet mount preparation, formaldehyde-ether sedimentation and Kato-Katz techniques were used to examine stool samples for *Ascaris* eggs, and prevalence was found to be 37.8%. On multivariate logistic regression analysis, factors significantly associated with *Ascaris* infections included living in attached houses, shared toilet facilities, de-worming period more than three months, maternal education level and living in the "top" government administrative division in the study area. As in the other studies from the estate sector, poor sanitation facilities and poor health education were found to be important factors associated with *Ascaris* infections.

Impact of control programmes on STH prevalence

Mass deworming programmes were widely pursued by public health authorities in Sri Lanka in the first half of the 20thcentury, even though the anthelmintics were not very effective.[12] More recently however, anthelmintics have not been used on a mass scale, except in relation to certain defined, target populations.

For example, a biannual mass deworming programme with single dose mebendazole (500mg) targeting school aged children was implemented in the plantation sector from 1994 to 2005, after it was shown that the prevalence of STH infection among these children was over 90%.[21] In 2009, five years after the deworming programme had been abandoned due to lack of funds, faecal samples from 1,890 children attending 114 estate sector schools in five districts (Kandy, Nuwara Eliya, Badulla, Ratnapura and Kegalle) were examined using single Kato-Katz smears.[22] Although the prevalence was nowhere near as high as in the 1990s, the overall combined prevalence was still high (29.0%), while 24.4% had ascariasis (found in all five districts), 5.9% had trichuriasis (also seen in all five districts), and 4.7% had hookworm infections (not found in Nuwara Eliya and Badulla districts). This study demonstrated that even after ten years of mass chemotherapy, prevalence can bounce back after cessation of preventive chemotherapy, if the initial force of transmission is strong and other long-term control measures are not concomitantly implemented.

The above results present a stark contrast with findings from the rest of the country. During the period 2002 – 2006, the mass drug administration (MDA) programmes conducted by the Ministry of Health to eliminate lymphatic filariasis (LF) as a public health problem from Sri Lanka, involved the annual administration of diethylcarbamazine citrate (DEC) and albendazole to all those living in the nine LF-endemic districts along the Western and Southern coastal belt. Since albendazole is very effective against STH infections too, several studies examined the effect of the LF MDA programme on STH infections.

In the first of these, children attending six selected schools in the Ragama Medical Officer of Health area were examined just before and after the MDA programme in July 2002.[23] Of the 265 children examined in the baseline survey, only 12 had any STH infection (prevalence 4.5%). In the follow-up survey only 2/252 children (2.0%) were infected. Like overall prevalence, the mean egg counts (as estimated by the examination of single Kato-Katz smears) also declined from baseline to follow up but the differences were not statistically significant in either event.

The second survey was conducted in 2006 to assess the impact of LF MDA in the Western Province.[24] Faecal samples from 448 children who attended 17 schools selected for the national survey conducted in 2003 (just after the 1st round of LF MDA) were examined using single Kato-Katz smears. Roundworm prevalence was found to be marginally lower in 2006 (4.0%) than in 2003 (4.7%), as was hookworm (0.2% vs 0.4%), whereas whipworm prevalence was higher (13.8% vs 9.4%). However, these differences, as well as that between the geometric mean egg counts, were not statistically significant. Compliance with MDA in 2006, however, as reported by the schoolchildren examined, was only 59%. The findings suggested that four annual rounds of MDA with DEC and albendazole had virtually no effect on STH infections among school children in the Western Province.

A third survey, conducted in 2012, explored the practicality of integrating surveillance for STH, (assessed by Kato-Katz) with transmission assessment surveys for LF in two evaluation units (EUs) in the Gampaha district.[25] Each transmission assessment survey tested children (N = 1,462 inland EU; 1,642 coastal EU) sampled from 30 primary schools. Low filarial antigenemia rates (0% and 0.1% for the inland and coastal EUs) suggested that LF transmission was very low in the Gampaha district. The STH rates were also low: 0.8% (inland) and 2.8% (coastal). Most STH detected were low or moderate intensity *T. trichiura* infections. The added cost of including STH testing was estimated at approximately $5,000 per EU, and the authors concluded that the results suggest that it is feasible to integrate school-based surveillance for STH and LF.

Drug resistance

Large-scale treatment with the benzimidazoles (albendazole and mebendazole) has been adopted globally as a major control strategy against STH infections. Prolonged and repeated treatment with the same anthelmintics has led to the emergence of widespread benzimidazole resistance in veterinary parasites, caused by a single nucleotide polymorphism at codon 200,167 or 198 in the β-tubulin gene.[26] Concern that prolonged use of these anthelmintics may select for resistant parasites has promoted efforts to develop genotyping assays to screen for β-tubulin polymorphisms in *N. americanus*. Single nucleotide polymorphism assays were developed based on the Smart amplification method (SmartAmp2) to target the above codons in the β-tubulin isotype 1 gene and applied to 110 *N americanus* larval samples from the Ratnapura district in Sri Lanka.[26] None of the larval samples showed significant levels of polymorphisms either at positions 167 or 200, but a polymorphism was identified at codon position 198A/C in some samples, the first time that this mutant type has been detected in *N americanus*. The results suggest that although full-blown benzimidazole resistance was not present in the samples tested, the mutations associated with its emergence are detectable.

Impact of STH infections on health

As summarized previously, the early literature from the last century bears ample testimony to the morbidity and even mortality caused by heavy STH infections: severe anaemia, reduction in physical fitness, acute intestinal obstruction, rectal prolapse, etc.[12] As prevalence rates and the intensity of infections have declined, these manifestations have become increasingly rare and in the current context, STH infections are often asymptomatic. As a result, the studies published over the last two decades on the association between STH infection and ill health have focussed on more subtle manifestations such as physical growth, anaemia and cognitive development in children.

During the national survey of the health status of school children conducted in 2003, children with STH infections were found to have a significantly higher prevalence of anaemia than those who were uninfected.[13] There was however no significant association between STH infection and stunting of growth as assessed by height for age z-scores and body mass index.

A prospective placebo-controlled randomized study was conducted in 2009 -2010 to assess the impact of de-worming and iron supplementation on the cognitive abilities and educational achievement of school-age children in the plantation sector.[27] The treatment group (n = 615) received de-worming (mebendazole 500 mg single dose) and weekly iron supplementation (tablets containing 200 mg of ferrous sulphate equivalent to 60 mg of elemental iron) for six months, while the control group (n = 575) received placebo for both the anthelmintic and iron. The prevalence of soil-transmitted helminth (STH) infection was reduced in the treatment group, with significant differences between treatment and control groups in the levels of *Ascaris* and *Trichuris*. The results also suggested that the anthelmintic treatment was effective against roundworm and whipworm infections, but not hookworm infection. In contrast to the prevalence of roundworm which dropped from 20.8% at baseline to 14.3% at follow-up 6 months later, and whipworm, which also dropped from 7.5% to 4.9%, hookworm infection rose from 5.5% to 8.0% in the treatment group. This is consistent with the evidence from other efficacy trials that mebendazole is not as effective in treating hookworm as it is in treating roundworm or whipworm infections.[28] Final analyses found no impact on haemoglobin levels, nor any significant impact on concentration levels or on educational test scores. The authors concluded that decline in STH prevalence alone, in the absence of improved haemoglobin status, produced no evidence of impact on concentration levels or educational test scores.

A study conducted in 2013, on 489 children aged 1-12 years, living on Uduwela tea estate in the Kandy District, examined the association between ascariasis and physical growth of the children.[29] The prevalence of ascariasis was 38.4% and most children (51%) had light intensity infections, 30% had infections of moderate intensity, and 19% had heavy infections. The prevalence of undernutrition was 61.7%; 45% per cent were underweight, while 24.1% and 21.5% of children were stunted and wasted respectively. No significant association was found between *Ascaris* infections status and undernutrition, but heavy intensity infections were associated with decreased values of weight-for-height z-scores (WHZ).

The commensal flora of the gut is known to play key roles in human health, including nutrient metabolism, protection against pathogens and regulation of both innate and adaptive immune responses. Given that the soil-transmitted helminths and the gut microbial flora share the same environment within the human host, it is thought possible that parasite-microbiota interactions may impact on the health of helminth-infected individuals. A study conducted on 76 subjects from 9 villages in four districts of Sri Lanka explored qualitative and quantitative differences between the microbial community profiles of those infected with one or more STH, and uninfected subjects and volunteers who had been subjected to regular prophylactic anthelmintic treatment.[30] High-throughput sequencing of the bacterial 16S rRNA gene, followed by bioinformatics and biostatistical analyses of sequence data revealed no significant differences in alpha diversity (Shannon) and richness between groups. However, beta diversity was significantly increased in infected and treated subjects when individually compared to uninfected volunteers. Among others, bacteria of the families *Verrucomicrobiaceae* and

Enterobacteriaceae showed a trend towards increased abundance in infected persons, whereas the *Leuconostocaceae* and *Bacteroidaceae* showed a relative increase in the uninfected and treated respectively.

Current control strategy in Sri Lanka

In 2012, the Family Health Bureau of the Ministry of Health issued a general circular letter (Number 02-172/2012) with guidelines for de-worming children and pregnant women in the community setting during the period 2013-2016.[31] These guidelines divided the country into areas of high risk (Uva, Sabaragamuwa and Central Provinces) or moderate risk (all other provinces), based on the national survey conducted in 2003[13], together with the 2009 survey in the plantation sector.[22] The guidelines recommend that all children in high risk areas should be treated twice a year with a single dose of mebendazole (500 mg), while children in moderate risk areas should be treated once a year.

The guidelines issued by the Ministry of Health address community-based de-worming of both children and pregnant women. The latter group is included because hookworm infections are known to result in iron deficiency anaemia, which has particularly adverse health consequences for pregnant women, and because the age prevalence of hookworm infections, unlike that of ascariasis and trichuriasis, continues to increase until adulthood. Hence the recommendation, first issued by the Ministry of Health in 1994, is that all pregnant women should be given a single dose of mebendazole 500mg after completion of the first trimester of pregnancy.[12]

In 2017, a second national survey of STH infections was conducted, which showed that overall prevalence has declined in all parts of the country, including the high risk communities in the estate sector and urban low income settlements.[32] Based on these findings, the Family Health Bureau is currently in the process of revising the de-worming guidelines issued by the Ministry of Health.

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