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(Review Article)

Eliminating intestinal helminthic infections among school children living with HIv in Nigeria: A review

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Abstract

Helminthic infections in HIV-positive children can lead to disability and reduced quality of life. This review focuses on intestinal helminthic infections among school children living with HIV in Nigeria. Integrating deworming into existing HIV care could further reduce HIV-related morbidity and mortality in this population. Increased awareness of helminthic co-infection burden is needed, and collaborative strategies between government and non-governmental organizations are essential to help HIV-positive children reach adulthood.

Keywords: Helminthic infection; HIV; Nigeria; School children

1. Introduction

An estimated 1.5 billion people globally suffer from intestinal helminthic infections, with Africa exhibiting the highest prevalence in children, followed by Asia, Latin America, and the Caribbean(1,2). In 2010, the WHO estimated 50 million new cases of invasive amoebiasis, resulting in 40,000-100,000 deaths(3). Parasitic Helminths is increasingly becoming prevalent in both industrialized and developing nations, particularly among AIDS patients and children under five. Intestinal parasitic infections significantly complicate the treatment and care of HIV-positive individuals(4). While HIV-tuberculosis co-infections receive considerable attention, the management of HIV co-infection with neglected tropical diseases, a common comorbidity, is often overlooked.(5) Recent research links intestinal helminths to approximately 39 million disability-adjusted life years (DALYs), underscoring the need to reduce DALYs associated with HIV and intestinal comorbidity in this vulnerable population(6).

2. Intestinal Helminths

Intestinal helminths, classified by host organ and external shape, include bisexual and hermaphroditic species(7). Categorization relies on the morphology of eggs, larvae, and adults(8). Key groups are flukes (trematodes), tapeworms (cestodes), and roundworms (nematodes)(8). Flukes are leaf-shaped flatworms, typically hermaphroditic (except for blood flukes), that use oral and ventral suckers for attachment(7). Their life cycle involves a snail intermediate host. Tapeworms are long, segmented, hermaphroditic intestinal worms as adults(1). Larval stages reside in extraintestinal tissues, forming cystic or solid structures. Roundworms are bisexual, cylindrical worms found in both the gut and extraintestinal locations(8). Intestinal helminth eggs in human feces contaminate soil in unsanitary conditions, leading to common infections by roundworms, whipworms, and hookworms (e.g., *Necator americanus, Ancylostoma duodenale*)(7). Worm infections can cause diarrhea, abdominal pain, appetite loss, malaise, and weakness. They may also lead to intestinal bleeding, diarrhea, or dysentery, contributing to childhood mortality and impaired school performance due to absenteeism(2).

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Helminthic infections primarily occur through ingestion of infective eggs (e.g., *Ascaris, Echinococcus, Enterobius, Trichuris*) or larvae (e.g., certain hookworms)(4). Some larvae penetrate the skin (e.g., hookworms, schistosomes, Strongyloides)(9). Transmission can also involve vectors that introduce infective stages via bites (e.g., filarial worms) or ingestion of intermediate hosts containing larvae(9). Therefore, infection risk is influenced by hygiene practices (fecal-oral transmission), environmental conditions favoring infective stages, food preparation methods, and exposure to insect vectors(7).

3. Treatment of intestinal helminths

Albendazole effectively treats pinworm, hookworm*, ascariasis, trichuriasis, strongyloidiasis, cysticercosis*, and hydatid disease due to its systemic action and ovicidal properties against hookworm, *ascaris*, and *trichuris* eggs, making it superior to Mebendazole. Mebendazole treats *ascariasis*, hookworm, pinworm, and *trichuriasis*; administer pills without regard to meals(2,9). Pyrantel pamoate treats hookworm, pinworm, and *ascariasis*, but not *trichuriasis* or *strongyloidiasis*, primarily targeting intestinal worms due to its low absorption(7). Pinworm requires a second dose after two weeks to prevent reinfection. Levamisole (or tetramisole), specifically the active isomer levamisole, is used for ascariasis. Ivermectin is used for *strongyloidiasis* and *onchocerciasis*. Niclosamide achieves high cure rates against *Taenia saginata* and solium (95%) and Diphyllobothrium latum (85%)(9). Piperazine treats *ascariasis* and pinworms, often curing *ascariasis*. Praziquantel is the preferred anti-H. nana medication and is also effective against D. latum, T. solium, and T. saginata in a single dose, demonstrating a 100% cure rate against T. saginata(2). Therefore, prompt helminth treatment helps to prevent or treat autoimmune illnesses due to helminths presence before and after autoimmune reactions(10).

It is also worthy to note that WHO recommends albendazole (400mg) and mebendazole (500mg): cheap, effective, and easily administered by non-medical staff(11,12). Safe, with negligible side effects in millions. WHO provides these to endemic countries for school children(11).

4. Effect of helminthic infection on a child’s health

Helminthic infections pose a significant threat to the health and well-being of children, with far-reaching consequences for their physical and cognitive development(13). These parasitic infections can substantially impede a child's growth trajectory, hinder their developmental milestones, and compromise their cognitive function, frequently resulting in malnutrition, anemia, and diminished cognitive abilities. Intestinal parasites can induce chronic intestinal blood loss, which in turn leads to iron deficiency anemia(13,14). Furthermore, STH infections can significantly reduce food intake due to decreased appetite and impaired nutrient absorption, contributing to a vicious cycle of malnutrition and weakened immunity(15).

4.1. Specific Effects of Helminthic Infections on Children:

- Growth and Development: Helminthic infections, with soil-transmitted helminths (STH) being the primary culprits, exhibit a strong and detrimental association with both stunting, characterized by a reduced height for a child's age, and wasting, defined as low weight for height(13). These growth impairments stemming from helminthic infections exert a significant impact on overall physical growth, potentially leading to long-term consequences for a child's physical capabilities and health(16). The interference with nutrient absorption disrupts the building blocks needed for healthy growth patterns(15).
- Malnutrition: Helminths actively contribute to malnutrition through multiple mechanisms. These parasitic worms can directly reduce the absorption of essential nutrients from the intestines, impair a child's appetite, leading to decreased food consumption, and ultimately contribute to the development of malnutrition(15). This nutritional deficiency further exacerbates the negative effects of the helminthic infection itself, creating a detrimental cycle that weakens the child's overall health and resilience(15). Furthermore, malabsorption interferes with the proper utilization of the nutrients even if the child has adequate intake(16).
- Anemia: Hookworms, in particular, possess a unique ability to cause chronic blood loss within the intestines of infected children(15). This sustained blood loss leads to a significant depletion of iron stores in the body, resulting in iron deficiency and the subsequent development of anemia(16–18). Anemia, characterized by a reduced number of red blood cells or hemoglobin, can cause fatigue, weakness, and impaired cognitive function, further hindering a child's ability to thrive and learn(15). The parasitic worms thrive at the expense of the child's blood and nutrients(19).
- Cognitive Impairment: Helminthic infections can have a profound and lasting impact on cognitive development(13). They can impair various aspects of cognitive function, including memory, attention span, and overall cognitive processing speed.(20) This cognitive impairment can directly affect a child's school

performance, potentially leading to decreased educational achievement and limiting their future opportunities(13). The fatigue and weakness brought about by anemia further impact cognitive function, leading to difficulties in concentration and learning(20). These children may find it difficult to keep up with their peers in school(13).

- Increased Susceptibility to Other Infections: Helminthic infections have the unfortunate consequence of weakening the immune system, rendering children more vulnerable to a wide range of other infections(19). This heightened susceptibility is particularly pronounced in regions where soil-transmitted helminths (STH) and other pathogens coexist and overlap(21). The weakened immune system is less capable of effectively fighting off invading pathogens, increasing the risk of co-infections and further compromising the child's health. The impaired immune response makes them more vulnerable to common illnesses that they could otherwise combat.(13)
- Increased risk of disease: Certain helminthic infections, if left untreated, can progress to severe complications that pose a significant threat to a child's health(22). These complications can include rectal prolapse, a condition where the rectum protrudes from the anus; intestinal obstruction, a blockage in the intestines that prevents the passage of food and waste; and severe anemia, a life-threatening condition characterized by dangerously low levels of red blood cells(23). These severe complications highlight the importance of early diagnosis and treatment of helminthic infections(20).
- Impact on immune response to vaccines: The presence of helminthic infections can significantly influence the immune response to vaccinations(22). These infections can interfere with the body's ability to mount an effective immune response to vaccines, potentially reducing their effectiveness and leaving children less protected against vaccine-preventable diseases(21). This interference can compromise the overall success of vaccination programs and undermine efforts to control infectious diseases. Repeated deworming is thus crucial for ensuring maximum vaccine effectiveness(21).

5. Helminths and human immunodeficiency virus (HIV)

Helminths, parasitic worms, interact with the human immune system in a manner distinctly different from that of HIV(23). While HIV actively destroys cells of the immune system, leading to profound immunodeficiency, Helminths primarily modify or modulate immune responses(24). This modulation is often subtle, such that most individuals harboring helminthic infections are unaware that they are even infected; they remain asymptomatic(10). The immune regulation induced by helminthic infections is a double-edged sword, capable of either benefiting or harming the course of other human illnesses(25).

Specifically, helminth infection has been observed to potentially improve the clinical manifestations of atopic illnesses, such as allergies and asthma, as indicated by several studies (26–28). Furthermore, helminths may ameliorate the inflammatory pathology associated with autoimmune diseases(24,27,29), suggesting a potential therapeutic role in these conditions. A protective effect against cerebral malaria has also been proposed, although this protection may come at the cost of hindering parasite replication itself (29,30). However, research examining co-infection with both helminths and malaria has yielded inconsistent results, leading to varying interpretations of the interaction between these parasites(28,29).

In the context of bacterial and viral infections, the immune modulation caused by helminths can be detrimental(23,31). The impaired replication and weakened control of bacterial or viral pathogens resulting from helminth-induced immune alterations may be harmful to the host(23,25). Conversely, HIV infection, known for its devastating impact on the immune system, significantly impairs the immune response to a wide array of infections. Moreover, in individuals with advanced HIV infection, the compromised immune system control can lead to increased hypersensitivity responses to certain medications(23,30). This highlights the delicate balance and complex interplay between helminths, HIV, and the human immune system in the context of various diseases(23).

6. Helminth elimination: a strategy for improving HIV outcomes in children

In 2001, a significant step towards global health improvement was taken when the delegates at the World Health Assembly reached a unanimous agreement and endorsed resolution WHA54.19(11). This resolution specifically and urgently called upon countries where parasitic worm infections are endemic to take serious action in combating these infections, with a particular emphasis on schistosomiasis and soil-transmitted helminths (STH(11,22,32). This marked a pivotal moment in the global effort to address the burden of these neglected tropical diseases(32).

The preferred strategy for tackling soil-transmitted helminth infections involves the use of empiric therapy(22). This approach entails presumptively treating all populations considered to be at risk of infection(11,22). This method is favored over test-and-treat strategies, where individuals are tested for infection before receiving treatment(32). The primary reasons for favoring empiric therapy are the low cost and high tolerability of deworming drugs(11,22). These medications are generally inexpensive to procure and administer, and they rarely cause significant adverse effects in those who receive them. Furthermore, a strategy that relies on testing before treatment is considered less cost-effective. This is due to the relatively high cost of available diagnostic tests and the fact that these tests may not always accurately detect the presence of infection, exhibiting poor sensitivity in some cases(11). Therefore, treating all at-risk individuals is deemed to be the most practical and efficient approach(33).

The core strategy for controlling soil-transmitted helminthic infections revolves around controlling the morbidity, or illness, associated with these infections(32–34). This is achieved through the periodic treatment of at-risk individuals who reside in areas where these infections are prevalent. The people considered to be at risk include several key demographic groups: preschool children, who are particularly vulnerable due to their developing immune systems and hygiene practices; school-age children, who are also at high risk due to their activities and exposure; women of reproductive age, including pregnant women in their second and third trimesters and breastfeeding women, as these infections can negatively impact both maternal and infant health; and adults engaged in certain high-risk occupations, such as tea-pickers and miners, who are frequently exposed to contaminated soil and water(12,35,36).

Helminthic infections are recognized to have a significant impact on the human immune system(11). They can modulate immune responses and potentially weaken the body's defenses against other infections and diseases(14,21). In individuals living with HIV, the implications of helminthic infections are particularly concerning. Some studies have indicated that these infections may lead to a reduction in the number of CD4+ cells, which are essential components of the immune system's ability to respond to HIV(11,23). A decline in CD4+ cell count can compromise a person's capacity to control HIV viral replication, potentially accelerating the progression of HIV disease(14,15,22). Therefore, the treatment of helminth infections in people living with HIV could yield important benefits beyond the improvements observed in the general population following deworming interventions(11). By addressing helminthic infections, the immune systems of individuals with HIV may be strengthened, leading to better control of the virus and improved overall health outcomes(11,21,33).

Deworming initiatives can be efficiently integrated into existing healthcare programs. This integration can take the form of combining deworming with child health days or vitamin A supplementation programs for preschool children, offering deworming alongside the Human Papilloma Vaccine (HPV) program for adolescent girls, or incorporating deworming into broader school health programs(11,21). This approach leverages existing infrastructure and resources to maximize the reach and impact of deworming efforts(11).

Recognizing the importance of addressing *strongyloidiasis*, the World Health Organization (WHO) has included the control of morbidity due to *S. stercoralis* as an objective for 2030(11,35). This ambitious goal is considered attainable due to the current availability of pre-qualified ivermectin at an affordable cost(37). Ivermectin is an effective medication for treating *strongyloidiasis*, and its affordability makes it accessible for large-scale interventions(38). The distribution of ivermectin can be efficiently organized through the existing platforms and networks used to control other soil-transmitted helminthiases(39). This ensures that the medication reaches the populations in need through established channels(38). To further refine the strategy and rigorously evaluate its impact, pilot interventions are currently in place(38). These pilot programs are designed to gather valuable data and insights that will inform the development and implementation of broader control efforts(34).

In 2021, a remarkable achievement was reached, with over 500 million children being treated with anthelminthic medicines in countries where these infections are endemic(11)(22). This impressive figure represents 62% of all children who are at risk of infection. Furthermore, more than 99 million women of reproductive age were treated with albendazole through lymphatic filariasis elimination programs(22,39). These efforts highlight the scale and scope of ongoing deworming initiatives(22). Between 2010 and 2019, a significant reduction in the burden of disease caused by STH was observed(22,38). The number of Disease Adjusted Life Years (DALYs) lost annually due to STH decreased by more than 50%(35). This reduction corresponds to the period during which preventive chemotherapy (PC) for STH was scaled up in endemic countries(15). The success demonstrates the effectiveness of preventive chemotherapy in reducing the morbidity associated with these infections(11).

To ensure the continued success of these programs, the World Health Organization (WHO) recommends that endemic countries conduct epidemiological assessments after 5 to 6 years of implementing preventive chemotherapy(22). These assessments are crucial for measuring the impact of the programs and identifying areas for improvement(22). The WHO recommends that programs aim for an effective treatment coverage of >=75%, meaning that at least 75% of the target population should receive treatment. Based on the findings of the epidemiological assessments, countries should adjust their treatment frequency as needed to optimize control efforts(11). The key indicators used to monitor the impact of these programs include the prevalence of any STH infection and the prevalence of moderate and heavy intensity infections(35). Monitoring these indicators helps to track progress and identify areas where interventions may need to be strengthened(11).

7. Interventions in for prevention and control of soil-transmitted helminthiases in Nigeria

Humanistic output 2030 global targets for soil-transmitted helminthiases in Nigeria include eliminating morbidity in pre-school and school-aged children, reducing the number of tablets needed for preventive chemotherapy, increasing domestic financial support, establishing an effective control program for adolescents, pregnant and lactating women, and establishing an effective system(11,22,40). The 2030 Neglected tropical diseases (NTD) roadmap requires WHO to work with Member States and partners with member countries like Nigeria to achieve and maintain effective preventative chemotherapy coverage for Soil-Transmitted Helminths (STH) in all at-risk groups, measure the impact of interventions in countries that have been implementing the program for more than 5 years, and advocate for STH control integration in primary health care (PHC) for program sustainability(22,41,42).

Nigeria, like other nations, is committed to achieving the World Health Organization's (WHO) ambitious global targets for addressing soil-transmitted helminthiases (STH) by the year 2030(11,22,41). These targets specifically aim to significantly improve the health and well-being of vulnerable populations within Nigeria. One crucial objective is the complete elimination of morbidity, meaning sickness and disease burden, associated with STH infections, particularly among pre-school children and school-aged children, who are especially susceptible to the negative effects of these parasitic worms(40). Another key target focuses on optimizing the use of medication by reducing the overall number of tablets required for preventive chemotherapy programs(12). This aims to make treatment more efficient and cost-effective(33). Furthermore, a crucial element of the WHO's strategy involves fostering greater ownership and sustainability through increasing the amount of domestic financial support dedicated to STH control initiatives within Nigeria(40). The plan also calls for the establishment of a robust and effective control program tailored to the specific needs of often-overlooked groups, including adolescents, pregnant women, and lactating women, recognizing their unique vulnerabilities and the potential impact of STH on their health and the health of their children(37). Finally, the WHO targets emphasize the importance of creating an effective system for monitoring, evaluation, and program management to ensure the long-term success of STH control efforts in Nigeria(32).

Aligned with the broader 2030 Neglected Tropical Diseases (NTD) roadmap, the WHO has a mandate to collaborate closely with Member States, including Nigeria, and various partner organizations to achieve and sustain effective preventative chemotherapy coverage for STH across all at-risk population groups(40). This necessitates a concerted effort to ensure that deworming medication reaches all those who need it. The roadmap also highlights the importance of rigorous monitoring and evaluation(11)(35). Specifically, the WHO is tasked with measuring the actual impact and effectiveness of interventions in countries, such as Nigeria, that have been consistently implementing STH control programs for a period exceeding five years(40). This data is vital for refining strategies and maximizing the impact of ongoing efforts. In addition to widespread treatment, the WHO emphasizes the need to advocate strongly for the integration of Soil-Transmitted Helminths (STH) control measures into the existing primary health care (PHC) system within Nigeria(11). This integration is seen as a crucial step towards ensuring the long-term sustainability of STH control efforts by making it a routine and accessible part of the overall healthcare infrastructure(22).

8. Current situation in provision of Helminths-infected school children living with HIV

In Nigeria, school-based deworming programs, despite WHO recommendations, are poorly implemented, leaving many Helminths-infected school-age children untreated(43,44). Children, especially those with HIV or those unable to attend school, are often excluded from these interventions, exacerbating illness and absenteeism(40,43). HIV-infected children are also less likely to receive other essential health services like complete vaccination(44). HIV care centers, serving as frequent points of contact for HIV-infected children and their families, currently offer a limited range of services(43). Integrating deworming into existing HIV treatment could further reduce HIV-related morbidity and mortality among these children(43).

9. What the evidence in this review suggests

In HIV-positive children, deworming without assessing helminthic infection may slightly reduce viral load at six weeks (low quality evidence), but repeated dosing over two years shows little or no effect on viral load (moderate quality evidence) or CD4+ cell count (low quality evidence), based on two studies(11,22). In HIV-positive adults with diagnosed helminthic infection, deworming may slightly suppress viral load at 6-12 weeks and modestly improve CD4+ cell count at 12 weeks (both low quality evidence)(11,22,32,33). However, these findings rely on small studies, particularly a single study on praziquantel for schistosomiasis, necessitating confirmation through further research across diverse settings and populations(11,22,34). Despite the positive effect recorded from deworming children of school age, adverse event reporting is poor (very low quality evidence), and trials were too small to assess mortality effects (low quality evidence)(22). Notwithstanding, deworming drugs do not appear harmful to HIV-positive individuals(22).

10. Conclusion

Treating and preventing helminthic infections in HIV-infected children may improve their response to HIV therapy. Integrating helminthic control into existing HIV care programs could further reduce morbidity and mortality in this vulnerable population. Despite poor implementation of deworming programs, governments should prioritize their integration into routine care. Policy implementation and monitoring at all HIV care levels are crucial, requiring adequate funding, monitoring, and follow-up mechanisms

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