MSD

Medical Science and Discovery
ISSN: 2148-6832

Prevalence and pattern of soil transmitted intestinal helminth infections amongst HIV infected children in a tertiary hospital south eastern, Nigeria

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ABSTRACT

Objective: Soil-transmitted helminth infections (STHI) coexist with human immunodeficiency virus (HIV) infection, and they are widespread in environments where poverty is endemic. Helminths upregulate immunological stimulation while HIV's effect is down-regulatory, depicted by the increased incidence of hypersensitivity drug reactions in advanced HIV/AIDS. Hypobiosis (a state of dormancy in the host with the capability of reactivation and establishing intestinal infection over long periods) among helminths is accentuated in the presence of a low CD4 count. This makes HIV-positive patients often have a higher load of helminths. The study sought to determine the pattern, prevalence, and specie specific prevalence of intestinal helminthiasis in children living with HIV and HIV seronegative controls.

Material and Methods: This was a comparative cross-sectional study, conducted amongst 256 sero-positive children, and 268 matched controls recruited into the study between October and December 2022. Subjects were excluded if they had been given any antihelminth in the six weeks preceding enrollment. Data were collected using a structured interviewer-administered questionnaire. Fresh stool samples were analyzed using the Kato-Katz method.

Results: The prevalence of intestinal helminthiasis in children living with HIV was 47.7% and 36.6% amongst the sero-negative control population (p = 0.7589). Among the subjects and controls, the highest prevalence was seen in the 5-9 year age group, while those over 15 years had the lowest prevalence. These differences in the prevalence of helminths infection amongst the various age groups were significant in the subjects only and not in the controls. Of all the STHI, Hookworm infection constituted the majority 52.5%. Multiple STHI were seen in 20.7% of subjects living with HIV, while 9.3% were seen in the control. The difference is statistically significant (p = .00003).

Conclusion: Soil-transmitted helminthic infection is more prevalent in children living with HIV than in apparently healthy children. Regular deworming should be considered in the care of children living with HIV.

Keywords: HIV, Soil-transmitted helminthic infection, Immunomodulation

Research Article

Received 23-05-2023

Accepted 17-06-2023

Available Online: 18-06-2023

Published 30-06-2023

INTRODUCTION

Human Immunodeficiency Virus infection (HIV) and acquired immunodeficiency syndrome (AIDs) described as Obiriajaocha in the local Igbo dialect, has emerged as a serious public health challenge (1). Since the beginning of the epidemic about 42 years ago (1981), 84.2 million people have been infected with the HIV and 40.1 million died of AIDs related complications (1). By the end of 2021, (1) 38.4 million people were living with HIV infection worldwide. The African region remains disproportionately affected (2). The Nigerian national prevalence of HIV infection is estimated at 1.4% (3). Twelve percent of people living with HIV infection are children aged 0 to 14, while 8% are adolescents aged 10 to 19(3). Children with HIV infection have reduced immune response resulting in increased risk of opportunistic parasitic infections (2). Significant enteropathy characterized by increased levels of mucosal inflammation, reduced mucosal repair and regeneration is a common finding; this results in poor mucosal protection against those parasites commonly checked by intact mucosa (4).

Over 1.5 billion people, or 24% of the world's population, are infected with soil transmitted infection worldwide (5). In Nigeria, prevalence ranges from 30.3% to 55.2% depending on the method of analysis of stool and location of study (6,7,8). Soil transmitted helminths include worms such as, Ascaris lumbricoides (round worms) Trichuris trichuria (whipworm) Ancyclostoma duodenale and Necator Americanus (hook worms). Others are Enterobius vermicularis or pin worm and Strongyloides stercoralis. It is most prevalent in the tropics and subtropical region of the world and in these areas, it is most prevalent in the poorest section of the population (6). Odinaka et al (9) put the prevalence of helminths infection amongst school aged children in a rural setting at 30.3%. Varied prevalence rates of 54.8%, 55.2% and 42.6% have been reported by other workers respectively (6,7,8).

Co-infections in children in the tropics: A significant proportion of Sub Sahara's population lives under poverty, lacking adequate sanitation and potable water, making them prone to infection with intestinal helminths. In rural, tropical and marginalized areas of the world especially in Africa, co-infection by multiple pathogens such as bacteria, viruses, protozoa and fungi is the rule rather than the exception (10). The outcome of these multiple pathogenic interactions is unpredictable; these outcomes may differ from one co-infection to another. It may be neutral, facilitative or antagonistic, resulting in increased host susceptibility to infection, increased severity to infection or impaired treatment efficacy (11). In sub–Saharan Africa, there is a geographical overlap between Human immunodeficiency virus (HIV) and intestinal helminths parasitic infection (10). While HIV destroys the immune system, helminths up modulate it. HIV infection impairs immune response to many pathogens and in advanced cases poorly regulates the immune response as illustrated by the increased incidence of hypersensitivity reactions.

Studies of the interaction between HIV infection and intestinal parasitic infections have suggested that HIV-infected patients who are coinfected with helminths experience a shift in their immune system from a T helper type 1 (Th1) response to a predominantly T helper type 2 (Th2) response as well as an increase in immune system activation (12). Also, the concomitant infection of HIV and intestinal parasites may potentiate the severity and progression of both within the infected person (12). Th1 cells are essential in eradicating intracellular pathogens, and inflammatory responses. Th2 cells, on the other hand, target extracellular pathogens and produce cytokines, which enhance antibody production. The increased Th2 and diminished Th1 responses as well as the chronic immune activation found in patients with intestinal helminth infection have been hypothesised to lead to an increased susceptibility to HIV infection and enhanced HIV replication in helminth-infected individuals (13, 14).

Though helminth infection rarely causes death, it impairs physical and mental growth, iron deficiency anaemia, malabsorption and malnutrition in children (10). This may result in a vicious cycle of malnutrition, infection and immune deficiency which may predispose individuals to HIV and further helminthes co infection; thus, maintaining the cycle of poverty and disease. There have been many locally published studies on the prevalence of helminth infection amongst children and limited among adults and yet fewer amongst HIV sero positive children.

MATERIAL and METHODs

Study design and setting: This was a cross sectional study comparing the prevalence, specie specific prevalence of intestinal helminthiasis of children with HIV infection on HAART attending the Imo State University Teaching Hospital paediatric HIV clinics and HIV negative children (controls) attending the outpatient clinics. The study was carried out between September 2022-December 2022. Imo State University Teaching Hospital is located in Orlu. Orlu is located in Imo state, South Eastern part of Nigeria; with annual rainfall varying between 1990 mm and 2200 mm. The mean annual temperature is about 27^0C with relative humidity of 75% (15). It is a tertiary health care facility which serves majorly as a referral centre for health facilities in Imo State and an alternate facility for the adjoining Anambra, Abia, and Rivers states. One hundred and fourteen HIV positive participants were recruited consecutively with matched controls giving a total of two hundred and twenty-eight subjects.

Inclusion and exclusion criteria: All HIV positive HAART experienced children aged 1 to 18 years, attending the paediatric HIV care clinic at IMSUTH were enrolled consecutively until the study sample size was attained. The controls were matched children, recruited from the outpatient clinic aged 1 year to 18 years and HIV negative (HIV testing is offered to all children seen in the outpatient's clinic). Subjects were excluded if they had been given any antihelminth in the six weeks preceding enrollment, or HIV positive (They are referred to the HIV care clinic). Those unwilling to participate or whose caregivers declined consent were also excluded and allowed to access care without hindrance.

Where sample size NO = $[Z^2(p)\ (1-p)]/d^2$

Corrected for a finite population of 200

$n = N_O$

$[1+ No]/N$

Z = Confidence interval of 1.96

D = Tolerable error, margin fixed at 0.05

N = Total population of patients with HIV infection attending the paediatric HIV clinic at IMSUTH Orlu = 200

$N_O = [3.84 \times 0.166 \times 0.834]/0.0025 \qquad = 212$

For a finite population of 200

n= 212/(1+212/200)= 102

Correction for 12% Non-response

No. $^{12}/_{100} \times 102 \ = 12.24$
Sample size = 102 + 12 = 114

The minimum sample size for this study is 102. This however was raised to 114 to allow for 12% non-response rate.

 http://dx.doi.org/10.36472/msd.v10i6.957

Data collection: Data was collected using pre-tested structured questionnaires. Information obtained included sociodemographic characteristics, environmental and medical history of the children. Stool analysis and microscopy was done for all samples. Fresh stool samples were collected from participants on the same visit, in sterile open mouthed, labelled universal containers. Those who could not, went home with the universal container and returned the sample the next day or next clinic day. Samples collected were analyzed, with microscopy done using the Kato-Katz method, that facilitates the detection and quantification of heminth eggs in the stool of infected subjects. The slide of the stool sample was read within 4-6 hours after taking the sample.

Data analysis: Data obtained was analyzed using the Statistical Package for Social Sciences version 21 (SPSS Inc Chicago, Illonis, USA). Biodata, socio-demographic and clinical characteristics were presented as frequency and percentages. Binary logistic regression was used to determine the associations between different variables and soil transmitted intestinal parasitic infections. Results were tested for significant association using the Chi square and were considered statistically significant if the p-value was less than 0.05.

Ethical Approval: Ethical approval for the study was obtained from the research and ethical committee of IMSUTH/CS/121. Written informed consent was obtained from all the participants and the assent of the 7 years and older child was obtained for the study. Subjects could be withdrawn from the study at any point with no negative consequence to the care they were receiving or would receive. Treatment was offered to patients diagnosed to have intestinal helminths. To ensure anonymity of the subject, codification of data was done.

RESULTS

Sociodemographic data: A total of 256 HIV positive subjects and 268 matched controls were recruited into the study. The age range was 9 months to 17.6 years for the subjects and 7 months to 18.3 years for the control.

In table I, the age group 5 to 9 years was the most represented in both subjects and controls. There was no significant difference in the age distribution between the subjects and controls ($\chi 2= 2.8718$, df = 3, p = .4118). Majority of subjects were males (143, 55.9%), in contrast majority of the controls were females (138, 51.5%). These differences in gender between subjects and controls were not statistically significant (Yates corrected; $\chi 2$ = 2.1850, df =1, p = .1395). The male female ratio of both subjects and controls are 1.08:1.00 and 1.00:1.06 respectively. Similarly, there was no statistically significant difference in the distribution of socioeconomic status between the subjects and controls (χ^2 = 2.2476, df = 2, p = 0.3251).

Relationship between the sociodemographic factors and Soil transmitted Helminths in the subjects and controls.

Table II shows the relationship between the sociodemographic characteristics of the subjects and controls. Amongst the subjects the age group most affected by STH infection is 5-9 years 46 (57.7%), while the least affected age group are those more than 15 years 16 (27.3%). In the control arm, the age group most affected by STH infection is 5-9 years 42 (45.7%), while the least affected age group are those more than 15 years 14(33.3%). These differences in the prevalence of helminthes infection amongst the various age groups were significant in the subjects only and not in the controls. With respect to gender, majority of those infected with STH amongst the subjects were males 65(45.5%), while majority of the controls infected were female 54(39.6%). The relationship between gender and the prevalence of STH infection amongst both subjects and controls as statistically insignificant. Socioeconomic class II (middle class) had the highest level of infestation 63(72.4%) among the subjects, while in the control arm, socioeconomic class III (lowest class) had the highest level of infestation 44(60.5%). While the least prevalence rate for helminthes infection in both the subjects and controls was observed in the SEC I 21(27.6%) and SEC II 26(25.6%) respectively. The relationship between socioeconomic class and the prevalence of STH infection in both subjects and controls was statistically significant.

Prevalence/distribution of helminth infection in both subjects and controls: The overall prevalence rate in the subjects is 47.7% much higher than 36.6% observed amongst the controls. Comparatively this difference in the prevalent rates of STH infections seen in both subjects and control was not statistically significant ($\chi 2$ = 3.1509, df = 1, p = .7589). This is shown in **Table III**.

The pattern of soil-transmitted Helminthes infection in both subjects and controls. Table IV shows the 122 subjects infected with STH, Hookworm infection constituted the majority 63 (51.6%); while Roundworm was the commonest 61(62.2%) STH amongst the controls. However, the differences in the pattern of STH infection between the subjects and controls were statistically significant ($\chi 2$ = 18.9776, df = 2, p = .00007).

Prevalence of multiple Soil transmitted Helminthes. Cases of multiple STH were seen in 53 subjects constituting 20.7% of STH infection, while 25 (9.3%) cases of multiple STH were seen in the control. This difference in the prevalence of multiple STH infection amongst subjects and controls was statistically significant ($\chi 2$ = 20.6065, df = 2, p = .00003).

Relationship between predisposing factors to STH and Soil-transmitted helminthes infection. **Table VI** shows the relationship between predisposing factors to STH and Soil transmitted helminthes infection amongst children with HIV (subjects) and children without HIV (controls) infection. When matched and compared, these differences were statistically significant for those who occasionally wear foot wears(Yates corrected $\chi 2$ = 17.2087, df = 1, p = .00003, OR = 2.64), those who use pit latrines(Yates corrected $\chi 2$ = 20.6285, df = 1, p = .00001, OR = 5.22), those whose source of water is piped borne water(Yates corrected $\chi 2$ = 8.6007, df = 1, p = .0034, OR = 4.15) from personal bore holes and those who wash their hands always after defecation (Yates corrected $\chi 2$ = 16.6968, df = 1, p = .00004, OR = 7.24). Logistic regression was applied to identify independent predictors of STH infection. Helminth infection was the dependent variable. The independent variables were wearing of foot wares, use of pit laterine and handwashing. The likelihood of being infected with STH, was higher amongst those that wear shoes occasionally (p value= 0.0003) pit laterine use (p = .00001), handwashing (p = .00004) in the HIV sero-positive respondents.

Table I: Sociodemographic characteristics of subjects and controls.

Sociodemographic characteristics	Subjects	Controls	df	χ^2	pvalue
Age (years)					
<4	60(23.4)	70(26.1)			
5-9	78(30.5)	94(35.1)			
10-14	63(24.6)	56(20.9)			
>15	55(21.5)	48(17.9)	3	2.8718	.4118
Socioeconomic status (SEC)					
SEC I	76(29.7)	85(31.7)			
SEC II	87(34.0)	102(38.1)			
SEC III	93(36.3)	81(30.2)	2	2.2476	.3251
Gender					
Male	143(55.9)	124(43.7)			
Female	113(44.1)	144(56.3)	1	2.1840	.1395
Total	256	268			

Table II: Relationship between Sociodemographic factors and Soil transmitted helminths infection in subjects and control

Demographic Factor	Subjects: N_o of participant Tested	Subjects: N_o participants infected	Subjects: χ^2	Subjects: Pvalue	Controls: N_o participants tested	Controls: N_o participants infected	Controls: χ^2	Controls: Pvalue
Age								
<4	60(100)	27(43.3)			70(100)	24(35.7)		
5-9	78(100)	46(57.7)			94(100)	42(45.7)		
10-14	63(100)	33(50.8)			56(100)	18(33.9)		
>15	55(100)	16(27.3)	12.3385	.0063*	48(100)	14(33.3)	4.4308	.2185
Gender								
Male	143(100)	65(45.5)			124(100)	45(43.7)		
Female	113(100)	57(50.4)	0.4455	.5045	144(100)	58(56.3)	0.4477	.5034
Socioeconomic Status								
SES I	76(100)	21(27.6)			85	28(32.9)		
SES II	87(100)	63(72.4)			102	26(25.5)		
SES III	93(100)	38(36.6)	35.3159	.00001*	81	44(60.5)	16.8842	.0002*

Table III: Distribution of Soil transmitted helminthes infection between subjects and controls

Soil transmitted Helminthes infection	**Subject %**	**Control %**
Infected Participants	122(47.7)	98(36.6)
None infected Participants	134(52.3)	170(63.4)
Total	256(100)	268(100)

Yates corrected chi-square $\chi 2$ = 3.1509 df= 1 p-value = .7589

Table IV: Pattern of Soil transmitted Helminths infection in subjects and controls

	Hookworm N_o (%)	Ascaris lumbricoides N_o (%)	Trichuris trichuria N_o (%)	N_0
Subject	63(51.6)	43(35.2)	16(13.1)	122
Control	24(24.5)	61(62.2)	13(13.3)	98

Table V: Pattern of multiple Soil transmitted helminths infection in subjects and controls

	Hookworm and Ascaris L n_o	Ascaris L and Trichuris trichuria n_o	Hookworm, Ascaris L and Trichuris Trichuria n_o	Total Multiple infection n_o
Subject	9(17.0)	10(18.8)	34(64.2)	53
Control	15(60.0)	7(28.0)	3(12.0)	25

$\chi 2$ = 20.6065, df = 2, p = 0.00003

Table VI: Effect of predisposing factors on soil-transmitted helminthes infection in both subjects and controls

Foot wear	HIV infected: Infected with Helminths	HIV infected: Not Infected with Helminths	Non HIV infected: Infected with Helminths	Non HIV infected: Not infected with Helmints	df	Yates corrected χ^2	Pvalue	CI	OR
Always	29	74	40	60	1	3.1527	0.07488		
Occasionally	89	64	63	105	1	13.0470	0.0003	(1.48,3.36)	2.32
Sewage disposal									
Water closet	53	58	63	44	1	2.7112	0.09964		
Pit latrine	41	48	14	75	1	19.1814	0.00001	(2.26,9.28)	4.58
Surface/bush	24	32	26	46	1	0.6022	0.4377		
Drinking water									
Sachet water	78	60	72	60	1	0.1067	0.7439		
Well water	17	51	20	61	1	0.00019	0.9654		
Bore holes	23	27	11	44	1	18.0860	0.0045	(1.44,8.08)	3.41
Washing hands									
Always	26	13	15	35	1	11.8561	0.0005	(1.9,11.47)	4.67
Occasionally	48	102	50	102	**1**	0.0276	0.8681		
Never	43	23	38	28	1	0.7988	0.3714		

DISCUSSION

The prevalence of intestinal helminths among the HIV positive subjects was 47.7% whereas that in the HIV sero-negative population was 36.6% and there was no statistically significant difference between the two-study population. The prevalence of intestinal helminths in our study is much higher than that obtained in an earlier study in Ebonyi State, Nigeria which documented a prevalence of 28.6% among HIV-seropositives and 20.2% in HIV-seronegatives (17). This difference in prevalence maybe explained by the fact that 100% of our subjects live in the rural areas and most of the subjects may have been treatment naïve to antihelminths. It may also be related to a relatively varying level of helminthes in different geographical locations, differences in methodology or host risk factors. However, prevalence rates reported by Mwambete et al (18) 47.5% in Tanzania is consistent with our findings. Although the prevalence of STH infestation was higher among the HIV seropositive subjects compared to the control, there was no significant relationship between HIV seropositivity and helminthiasis. Our finding was comparable with Orji et al. (17) Low immunity among HIV positive subjects predisposes them to intestinal opportunistic infections leading a higher prevalence of intestinal parasites compared to HIV negative subjects. This may account for the higher prevalence seen amongst HIV sero positive subjects in our study. In areas where the risk of getting intestinal helminths is high, it is important that HIV patients are tested and connected to HAART. HIV care, treatment centers must integrate treatment of intestinal helminths in high-risk rural areas as part of routine care, especially for newly enrolled clients. This is in line with the UNAIDS 2025 targets which emphasizes that 90% of people living with HIV are linked to context specific-integrated services (19).

It was observed in this study that children aged 5 to 9 years (primary school age) had the highest prevalence rate of infection with soil transmitted helminths, while children aged 15 years (Secondary school age) and above had the least in both subjects and controls. Similar pattern of helminthes infection in relation to age was reported by other workers such as Orji, (17) Odinaka (9) and Salawu et al. (20) Health education, sanitation, personal and environmental hygiene are the most important ways to preventing STH infection. Older children of secondary school age can easily adhere to instructions on how to reduce soil contamination and are more mindful of their personal hygiene.

There was no statistical predilection of STH infection for gender observed in this study. However, the study noted a higher prevalence rate amongst the male subjects in contrast to a higher prevalence rate amongst the female controls. This may be explained by the adventurous nature of the male coupled with their being HIV sero positive being associated with some form of neglect in family. Maybe the preference for the male child may be responsible for neglect of the female control subject, particularly in the rural areas. Orji et al in Abakalike (17) and Salawu et al (20) in Ibadan noted a higher prevalence rate amongst the male gender. Gender interacts with various socioeconomic factors and biological determinants in the developing countries to create different health outcomes for males and females (20,21).

Majority of children in these studies (82.7%) with HIV infection who had STH infection belong to the lower socioeconomic class. This same pattern was observed in the control. Low socioeconomic status and its correlates such as lower educational attainment, poverty, poor nutritional status, reduced accessibility to health care ultimately affects the rate of infection with STH (19).

In this study, Hookworm infection had the highest prevalence amongst the HIV positive subjects. This is in keeping with findings from other studies (17,22) carried out on children with HIV infection. In contrast Ascaris lumbricoides had the highest prevalence rate amongst the controls. This difference in the pattern of helminthes infection between children who are infected with HIV and those not infected with HIV was statistically significant. The high prevalence of hookworm as observed could be, because hookworm infection is associated with low CD4 T cell counts which may exaggerate the dormant state in muscle and intestine making elimination from the body difficult in children with HIV, though mainly in adult patients with HIV infection (22). An adult hookworm on the average may stay up to 4 years in the body; due to hypobiosis (a state of dormancy in the intestine or muscle of the host and is capable of reactivating and establishing intestinal infection over long periods of time).

This state is heightened in the face of immune suppression as seen in these HIV seropositive children. A significant finding in this study is the high prevalence rate of multiple soil transmitted helminthes infection especially amongst children with HIV. This is keeping with findings of studies that state that polyparasitism has been associated with presence of high intensity of STH infection and low CD4 counts in individuals (23).

Using logistic regression, occasional use of foot ware, defecating in a pit laterine, infrequent handwashing lack of borehole water use were shown to be independent predictors of STH infection. These variables tend to protect children against STH. This study's observations also highlight that HIV predisposes these children to soil-transmitted infections. This may reinforce the theoretical belief that HIV infection may predispose participants to increased risk of Helminthes infection. This finding has been noted by Orji et al (17). Though, most of these findings were in adults (22).

Routine administration of antihelminthics should be considered in the care of children living with HIV in the care and treatment clinics. This will go a long way in reducing the morbidity and mortality associated with HIV/helminth coinfection.

Limitations: This study is a single-center, hospital-based study with small sample size. A multicenter, multi-regional study may need to be done to be able to generalize on our findings.

CONCLUSION

Helminths infection is common amongst HIV infected children seen in Imo State University Teaching Hospital Orlu. It is important that screening for helminths is routinely carried out in the HIV care clinics and treatment given appropriately and regularly in our resource-poor setting. It should also be included in the HIV care programme of children.

Acknowledgements: The authors appreciate the staff of the HIV care clinic of IMSUTH for their support in carrying out this work.

Conflict of interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author Contributions: JE, JO: Data Collection, design of the study**, JE:** manuscript preparation, revisions. All the authors have read, and confirm that they meet, ICMJE criteria for authorship.

Ethical approval: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and/or with the Helsinki Declaration of 1964 and later versions.

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