Original Research Article

Management of Helminthiasis and Virological Outcomes Among HIV coinfected Under-fives Receiving Health care at Mwananyamala Hospital, Tanzania

ABSTRACT

Background: Helminthiasis (HL) is a parasitic infection caused by worms that are contaminant to human body parts. The disease affects different regions of the world, but it is more prevalent in sub-Saharan African countries. A strong association between immunological status and helminthiasis among under-fives living with HIV infection (ULHI) has been reported.

Aim: The study aimed to assess the management of helminthiasis and virological outcome among ULHI receiving health care at the Care and Treatment Centre (CTC) located at Mwananyamala Regional Referral Hospital (MRRH) in Dar es Salaam, Tanzania.

Methodology: This was a retrospective and descriptive cross-sectional study involving scrutiny of the clinical records of ULHI, who sought medical attention at MRRH. The clinical records were randomly selected and examined, focusing on the prevalence rate of HL, the co-management of HIV and HL infections, the virological outcome based on the HIV viral load, and other relevant data.

Results: A total of 499 ULHI were involved; of those, 254 (50.9%) were females and 245 (49.5%) were males. About 49% of the ULHI had HL. The prevalence of HL and the age of ULHI were both associated with the virological outcome (HVL). ULHI with lower HVL had a relatively greater HL prevalence. The most widely utilized anthelmintics were ABZ, MBZ and IVE, in that order. The most frequently prescribed drugs for co-infections were ABZ-ALL and MBZ-TLD combinations.

Conclusion: Helminthiasis is still prevalent among ULHI, despite the lack of a significant difference between males and females. The prevalence of HL was relatively higher among ULHI with virological success (lower HVL).

Keywords: Helminthiasis, HIV infection, under-five children, virological outcomes

1. INTRODUCTION

Human immunodeficiency virus (HIV) infection is considered one of the leading causes of death among children under five years old in countries with a high prevalence of HIV infection. Globally more than 90% of all HIV infections among children are caused by vertical transmission from infected mothers during gestation, delivery, postpartum, and breastfeeding [1, 2]. In Tanzania, data on mothers and newborns infected with HIV using antiretroviral therapy (ART) scaled up from 2010-2018 [3]. However, linkage to care after diagnosis remains one of the weakest points of the national HIV infection prevention and control programmes [3-5]. Medical attention and adherence to ART in years after diagnosis of HIV infection are still one of the stumbling blocks in the health care system in our country. Of the numerous influencing factors, stigma and coverage of healthcare delivery plays a main role in this vast country [6,7].

Helminthiases are common infections caused by soil-transmitted helminths, namely *Ascaris lumbricoides, Trichuris trichiura, Necator americanus, Ancylostoma duodenale,* schistosomes and filarial worms which infect more than one billion people worldwide, rivaling HIV and malaria [8, 9]. The disease is very prevalent in Sub-Saharan African countries such as Tanzania, where the infections are more prevalent among ULHI due to deteriorated capacity to fight infections [10-13]. Generally, HL is one of the neglected tropical diseases and therefore lacks more stringent measures to fight parasitic HL-associated infections [14-16]. Several clinical complications may arise as a result of chronic HLs, such as abdominal pain and diarrhea, inflammation of the bile duct system, liver abscess, acute pancreatitis, appendicitis and suffocation are common [17, 18].

It is still unknown whether HLs impact determining variations in susceptibility to HIV infection [11,14]. However, it is evident that immune deficiencies with various etiologies can affect parasitic infections in diverse ways [19,20]. Strongyloidiasis is a case where this is more obvious because HIV co-infection has the opposite effect on parasite growth than other types of immunosuppression, like immunosuppression medications [21, 22]. Therefore, the purpose of this research was to evaluate HL management among HIV co-infected under-five children and its relationship to virological outcomes.

2. METHODOLOGY

2.1. Study design and population

This was a retrospective cross-sectional study conducted between November 2020 and April 2021 in the CTC health care at MRRH. The study population consisted of children under-fives years of age living with HIV and treated with ARV for 22 months (January 2019 to October 2020).

2.2. Data collection and statistical analysis

A sampling frame of 680 medical records was per-determined based on time and availability of resources. Each file was assigned one number between one and 680, and then 499 files were randomly picked using the Random Number Generator software. Each file was analyzed focusing on the following key aspects: demographic characteristics, diagnosis, viral load, ART, usage of the anthelmintic, presence of HLs, amount of visits/attendance at the CTC and other relevant information related to the study's aim were recorded. Data were analyzed by using SPSS version 22 software. Descriptive statistics, one-way ANOVA, logistic regression and Pearson's correlation, were performed to determine the correlation and association among the analyzed dependent and independent variables. Differences among individuals and between groups were regarded as significant when $p < .05$.

2.3. Exclusion and inclusion criteria

Only data within the specified period was collected. Files that missed more than two of the investigated variables were excluded. Only files of patients aged between one year and five years old were included. Files without a specific date of initiation of ART and the last visit to the CTC were excluded.

2.4. Ethical consideration

The ethical clearance was sought from the MUHAS Research and Publications Ethical Committee, preceded by approval from the School of Pharmacy Research Dissemination Committee. Permission to access the medical records was then obtained from the MRRH authority. Confidentiality was strictly observed by not disclosing the collected personal information.

3. RESULTS AND DISCUSSION

[In the present study, a total of 499 ULHI between 1 and 5 years of age attending CTC at MRRH in Dar es Salaam were enrolled. Of those, 254 (50.9%) and 245 (49.5%) were females and males, respectively. Virological failure was considered to have occurred when HVL exceeded 1000copies/mL in two consecutive measurements within a 3-month interval with adherence support after at least six months of following ART [23, 24]. ART failure is now recognized as associated with virological, immunologic, and/or clinical failure [24–26].

Slightly less than half (48.9%) of the studied ULHI were co-infected with HLs. Our findings coincide with those of a previous study conducted over a decade ago in Tanzania, indicating that half of the studied population of ULHI harboured

HLs [10]. In line with our most recent results, there were no appreciable variations in the prevalence rates of HLs between male and female ULHI nor among age groups of ULHI, as depicted in Table 1. Contrary to our observations, a study from Rwanda found that male children had higher prevalence rates than female children [27]. Likewise, a significant association between the prevalence of HL and the age of ULHI was observed (X^2 = 7.828; df = 2; p = .02). This coincides with studies done in Uganda that suggest that HLs increase with age [28].

Table 1: Characteristics of the study population and prevalence of HLs

Variables		***Contracted HI (%)***		***P-value (X^2)***
		No	***Yes***	
Sex	***Female***	***121 (24.25)***	***133 (26.65)***	***0.140***
	Male	***134 (26.85)***	***111 (22.24)***	
Age group	***0-2***	***6 (1.2)***	***19 (3.8)***	
	3-4	***59 (11.8)***	***56 (11.2)***	***0.02***
	5-6	***190 (38.1)***	***169 (33.9)***	
Attendance to CTC (months)	***1-2***	***219 (43.9)***	***142 (28.5)***	
	3-4	***28 (5.6)***	***72 (14.4)***	***0.001***
	5-6	***8 (1.6)***	***30 (6.0)***	

HIV-infected children face a lifetime of treatment because of the persistent nature of HIV. Several studies indicate that the earlier effective combination ART is initiated, the smaller the size of the HIV reservoir and/or viremia [24, 29]. Our findings showed no association between the sexes of ULHI and HVL. However, a statistically significant association was revealed between the prevalence of HLs and HVL (X^2=195.120; df = 471; p < .01), as indicated in Table 2.

Table 2: Contraction of HLs in relation to virological outcome (HVL) among ULHI

Virological outcome (Cut off 1000 copies/ml)	**Contracted HI (%)**		**Total**
	No	**Yes**	
Success	163 (73.1)	251 (100.0)	414 (87.3)
Failure	60 (26.9)	0 (0.0)	60 (12.7)
Total	223 (47.0)	251 (53.0)	474 (100.0)

According to the research, the majority of ULHI (87.3%) had virological success, which is less than the threshold of 1000 viral plasma copies per cubic millimeter, as shown in Table 3. Given that the majority of them (73%) frequently received medical care, this might be the result of their high CTC attendance. Time-lapse or attendance at CTC was found to be statistically significantly correlated with the frequency of HL (p-value = .01). The frequency of visiting the CTC was inversely correlated with a decline in the prevalence of rates of HL (contraction of HLs).

A regular CTC attendee, had a 2.079 times lower risk of developing HLs (p< .01). Nevertheless, between HL-infected and uninfected ULHI, the effects of CTC attendance and the virological outcome were similar (Figure 2). While there was a negative association (Pearson's R = -0.217; p < .01) between virological outcomes (HVL) and trends of CTC attendance.

Table 3: Usage of antihelminthics and HVL among the ULHI

Virological outcomes (copies/ml)	Antihelminthics (%) n=474*				
	None	**ABZ**	**IVE**	**MBZ**	**P-value**
Success (0-1000)	161(34.0)	216 (45.5)	19 (4.0)	18 (3.8)	
Failure (>1000)	60 (12.7)	0 (0.0)	0 (0.0)	0 (0.0)	
Total	221 (46.7)	216 (45.5)	19 (4.0)	18 (3.8)	0.001

(*) A total of 25 (5%) of the children had no records of HVL.

Slightly less than half (48.9%) of the ULHI under study had HLs as well. Our results support those of earlier research carried out in Tanzania more than ten years ago, which found that HLs were present in half of the ULHI population [10]. In our study, more than half (51.7%; n = 253) of the ULHI were taking prophylactic antihelminthic medication. The majority of them (85.4%) used ABZ. (Table 3). An association was observed between antihelminthics usage in relation to age group and virological outcome/HVL (X^2 = 23.281; df = 6; p = .001). The majority (88.0%) of the ULHI with low HVL were taking prophylactic antihelminthics (ABZ, MBZ, and IVE). Of 499 ULHI, 12% (n = 60) had HVL higher than 1000 copies per millimeter square (Table 3). The co-infections with HIV and HLs were regularly treated by ABZ-ALL and MBZ-TLD. But TLD was combined with all three antihelminthics. ULHI receiving a combination of MBZ-ZLL/R, ABZ-TLD, and IVE-TLD exhibited a low HVL (virological outcome) as depicted in Figure 1.

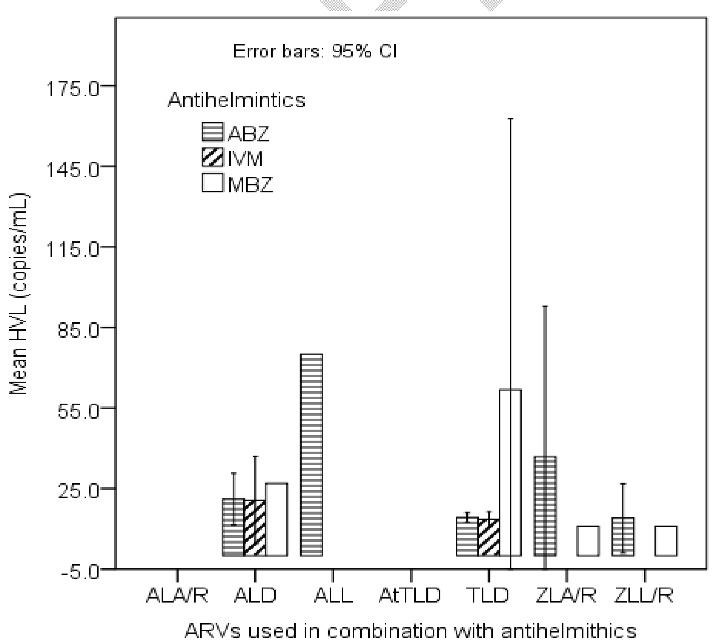

Figure1: Co-management of helminthic and HIV infections among the studied ULHI

Key: ALA/R - Abacavir, Lamivudine, Atazanavir/Ritonavir; ALD – Abacavir, Lamivudine, Dolutegravir; ALL- Abacavir, Lamivudine, lopinavir; TLD-Tenofovir, Lamivudine, Dolutegravir; ZLA- Zidovudine, Lamivudine, Abacavir; ZLL/R- Zidovudine, Lamivudine, Lopinavir /Ritonavir

Our study showed that ULHI treated with ART and anthelmintic had better virological outcomes (lower HVL) than those treated with only one therapy. Low HVL, a marker of virological success, points to higher amounts of CD4+ T cells, which typically regulate the immune system's regular operation. It is also recognized that anthelmintic therapy significantly improves ART in terms of immune function and viral replication prevention [30]. Contrary to the WHO's recommendation, IVE was administered to some patients in this research. The WHO recommends using ABZ, MBZ, levamisole, and pyrantel for the treatment of human HLs [31]. Several animal and human viruses, have shown susceptibility to the broad-spectrum antiviral action of ivermectin [32]. This partly explains the observed success in virological outcomes among ULHI treated with a combination of IVE-TLD in our study. TLD was the most commonly used ART combination, and ULHI getting TLD therapy showed improved virological results (lower HVL) coinciding with the previous observation by [33].

Despite this close pathophysiological relationship, there is a general dearth of information on how HIV and HLs interact, particularly in the era of widely accessible ART [11, 12, 34]. The prevalence rate of HLs was slightly higher among ULHI, who had lower HVL (Tables 2 and 3). It was observed that 206 ULHI had just initiated the ART at the CTC, which also featured as the first month of visit. Of those, 43 (20.9%) of the ULHI manifested virological failure. A total of 37 ULHI had not been to CTC in more than four months, but none manifested virological failure (Figure 2). In the study population, there was a clear correlation between the number of CTC visits and HVL (X^2 = 86.83; df = 30; p 0.001).

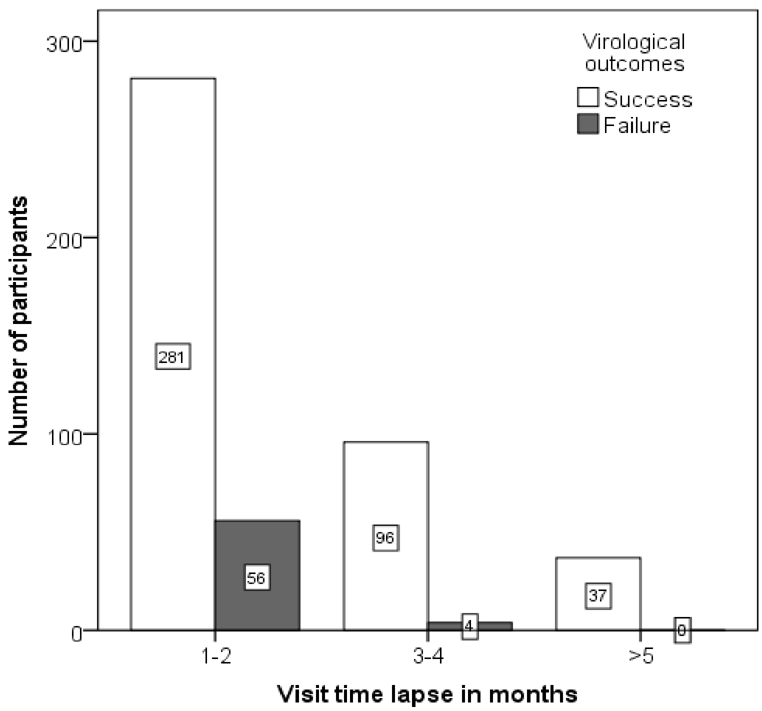

Figure 2: **Virological status among ULHI in relation to the length of visits to CTC**

HLs may inhibit the Th1 cell response directly, resulting in a decrease in CD8+ cytotoxic T lymphocytes (CTL), which are required to combat HIV [11]. In humans, the virological outcome is directly linked to HIV-specific CTL responses, and a decrease in CTL responses is associated with a faster progression of HIV infection [10]. It's possible that changes in immune regulation caused by HIV replication will produce more visible changes in HVL levels after HL or eradication. This could explain why 12.7% of ULHI who were not taking antihelminthics experienced virological failure.

In this instance, the observed high rate of HLs among ULHI with virological success (low HVL) could be attributed to cellular immunity activation (CTL). Numerous investigations on the relationship between HIV/AIDS and HL have currently produced contradictory results [10, 13, 33]. One of the characteristics of HIV infection, which is widespread and closely matches people with HLs, is chronic immune activation [11, 13]. As a consequence, ULHI with HL will unquestionably experience a quicker decline in health and may develop AIDS earlier [10, 13].

4. CONCLUSION

Helminthiasis is still prevalent among ULHI, albeit with no significant statistical difference between males and females. ULHI that experienced virological success (lower HVL) were more likely to acquire HLs than those that did not. ABZ-ALL and MBZ-TLD were the most frequently used combination therapies for managing HL-co-infected ULHI. The virological success was achieved using the combination of MBZ-ZLL/R, ABZ-TLD, and IVE-TLD. ULHI, who frequently visited the CTC for medical care, experienced a marked decline in HLs. Anthelmintic prophylactic chemotherapy should be given to ULHI more regularly to avoid HLs and enhance the well-being of the children. Studies need to be conducted to determine how HLs affect the decline in virological outcomes observed in the current study. We recommend comparing ULHI and HIV-negative under-fives to look into different factors that may shed light on some still-unresolved issues.

ETHICAL APPROVAL (WHERE EVER APPLICABLE)

Authors may use the following wordings for this section: "All authors declare that 'written informed consent was obtained from the School Research Committee and the University Clearance Ethical Committee (Institutional Review Board). Consent was obtained from hospital authorities and no names or personal information were disclosed.

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DEFINITIONS, ACRONYMS, ABBREVIATIONS

ABBREVIATIONS:

ULHI - Under five living with HIV infection
HL- Helminthiasis
CTC - Care and Treatment Centre
MRRH - Mwananyamala Regional Referral Hospital
HVL- viral load (virological outcome)
ARV- Antiretroviral
ART-Antiretroviral therapy
ABZ- Albendazole
IVE- Ivermectin
MBZ- Mebendazole
ALA/R - Abacavir, Lamivudine, Atazanavir/Ritonavir;
ALD – Abacavir, Lamivudine, Dolutegravir
ALL- Abacavir, Lamivudine, lopinavir
TLD-Tenofovir, Lamivudine, Dolutegravir
ZLA- Zidovudine, Lamivudine, Abacavir
ZLL/R- Zidovudine, Lamivudine, Lopinavir /Ritonavir