

Article

Impaired Anti-Schistosoma Seroreactivity in Advanced HIV Infection: Findings from a Cross-Sectional Study in Ghana

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Abstract

This study assessed the diagnostic reliability of anti-*Schistosoma* serology in Ghanaian patients with and without concomitant human immunodeficiency virus (HIV) infection. Serological testing was performed on serum samples containing PCR-confirmed *Schistosoma* spp. DNA using a commercial enzyme-linked immunosorbent assay (ELISA; EUROIMMUN, Lübeck, Germany). Following real-time PCR confirmation of either *Schistosoma mansoni* or *Schistosoma haematobium* complex DNA, samples were subjected to anti-*Schistosoma* IgG and IgM serology in duplicate. Results were qualitatively interpreted as positive, uncertain, or negative; reproducible positive results across test runs were defined as “consistent,” while all other profiles were classified as “inconsistent”. Serological consistency was then correlated with patient demographic and clinical data, including age, gender, HIV status, CD4+ and CD8+ T-lymphocyte counts, CD4+/CD8+ ratios, and HIV viral loads. Of the 41 individuals with PCR-proven schistosomiasis (*S. mansoni*, $n = 36$; *S. haematobium*, $n = 5$) and no clinical signs of Katayama syndrome, 39 were HIV-positive. Among these 39 coinfecting patients, consistently positive serology was recorded in 27 (69.2%) cases for IgG and 31 (79.5%) cases for IgM. Consistent IgG seropositivity was significantly associated with higher CD4+ (293 vs. 58 cells/ μ L, $p = 0.009$) and CD8+ (981.5 vs. 306 cells/ μ L, $p = 0.007$) T-lymphocyte counts. The association between higher CD4+ cell counts and consistent IgG reactivity remained robust in multivariable analysis (adjusted odds ratio = 2.04 per 100 cells/ μ L, $p = 0.01$). A non-significant trend in the same direction was observed for anti-*Schistosoma* IgM, whereas no other significant associations with epidemiological or medical factors were identified. In conclusion, the state of cellular immunity critically influences the reliability of serological schistosomiasis diagnostics in HIV-positive individuals. For patients with



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severe cellular immune depletion and suspected schistosomiasis, alternative diagnostic approaches, such as highly sensitive real-time PCR, should be strongly considered.

Keywords: schistosomiasis; serology; HIV; human immunodeficiency virus; AIDS; acquired immunodeficiency syndrome; diagnostic accuracy; immunosuppression

1. Introduction

Affecting over a quarter of a billion people in tropical endemic regions [1], schistosomiasis ranks among the most prevalent systemic parasitic diseases worldwide. The causative agents are trematodes of the genus *Schistosoma* spp., with clinical manifestations depending on the infecting species: *S. mansoni* and *S. japonicum* complexes typically cause intestinal and hepatosplenic schistosomiasis, whereas the *S. haematobium* complex leads to urinary schistosomiasis [2]. In travelers and migrants returning from endemic areas who present with eosinophilia, schistosomiasis must be considered a primary differential diagnosis [3].

Transmission occurs through skin contact with parasite-infested freshwater in endemic environments [1]. Acute schistosomiasis, also known as Katayama syndrome, is characterized by flu-like symptoms [2]. However, the clinical presentation of chronic schistosomiasis can vary widely, often featuring mild, intermittent, or nonspecific symptoms [2]. Standard treatment involves single or multiple doses of oral praziquantel to eradicate adult worms [2]. The clinical efficacy of praziquantel has recently been shown to be independent of the presence or absence of acquired immunodeficiency [4,5], yielding an expected cure rate of approximately 80% [6].

Diagnosis relies on a combination of microscopy, molecular biology, antigen testing, and serology. Because each method independently exhibits imperfect diagnostic accuracy, a combined diagnostic approach is often required [2]. Various serological assays utilizing different antigen types are currently in clinical use [7]. However, major limitations of serology include the delayed emergence of anti-*Schistosoma* antibodies and the inability of these tests to reliably distinguish between acute, chronic, and past infections [8]. Furthermore, a recent review highlighted the highly variable diagnostic accuracy of these antibody assays, reporting sensitivities ranging from 71% to 99% and specificities from 6% to 100% [9]. While the sensitivity of *Schistosoma* serology is generally considered superior to its specificity, it is hindered by broad confidence intervals, particularly when validated against composite reference standards [10,11]. A lack of assay standardization and broad validation remains a primary driver of this diagnostic uncertainty [9].

The interplay between human immunodeficiency virus (HIV) infection and schistosomiasis has been widely debated, with studies indicating increased odds of HIV positivity among individuals with schistosomiasis [12,13]. Furthermore, coincident schistosomiasis has been linked to higher HIV transmission rates and accelerated disease progression [14]. Although the exact reasons and directionality of these associations remain partly unclear [12], several underlying mechanisms have been identified. Specifically, *S. mansoni* infection alters anti-HIV immune responses, leading to the reduced detectability of bi-functional (IFN γ + IL-2- TNF- α +) CD4+ T-cells, heightened CD4+ T-cell activation, and diminished anti-HIV antibody-dependent cellular cytotoxicity (ADCC) titers [15]. Additionally, soluble egg antigen (SEA) from *S. mansoni* reduces the susceptibility of T-cells to CCR5-tropic HIV-1 [16]. In a Chinese cohort coinfecting with HIV and *S. japonicum*, patients exhibited reduced CD4+ T-cell counts and CD4+/CD8+ ratios, alongside elevated CD8+ T-cell counts [17]. Cross-reactivity has also been documented between antibodies targeting HIV-1 envelope glycoproteins (env) and *S. mansoni* glycan antigens [18–20], as

well as between anti-*S. mansoni* antibodies and the HIV virion infectivity factor (vif) [21,22]. Consequently, immune responses directed against schistosomiasis have been linked to false-positive HIV serology [23]. Notably, egg shedding is often reduced in HIV-coinfected schistosomiasis patients compared to their HIV-negative counterparts [24]. In patients progressing to acquired immunodeficiency syndrome (AIDS), the initiation of antiretroviral therapy (ART) can trigger a schistosomiasis-associated immune reconstitution inflammatory syndrome (IRIS) [25]. Conversely, schistosomiasis has also been shown to negatively impair HIV-specific immune responses [26].

Schistosomiasis inherently induces significant systemic immune alterations [12]. The disease typically elicits a slow adaptive immune response, even in immunocompetent hosts, and despite extensive research, no licensed vaccine is currently available [27]. Inflammation is primarily driven by tissue-deposited trematode eggs rather than the adult worms residing in the host's vasculature [28]. Embedded within tissue granulomas, *Schistosoma* spp. eggs provoke a CD4+ T-cell-dependent hypersensitivity reaction, where the balance between T-helper 1 (Th1) and Th2 responses determines the severity of the inflammation and subsequent disease [28]. A dominant Th1 response is associated with intense local inflammation and disease progression, whereas a Th2 response exerts antagonistic, tissue-protective effects [28]. However, this Th2-mediated reduction in host tissue damage represents a double-edged sword, as it simultaneously promotes parasite survival [29]. When considering worm rather than egg antigens, pronounced $\gamma\delta$ T-cell responses are elicited, which can be further modulated by co-existing active or latent tuberculosis [30]. Interestingly, unisexual infection models have revealed sex-specific immunological host responses: while male worms provoke strong innate immunity that ultimately reduces worm and tissue egg burdens, female worms suppress the early innate immune response to invading cercariae and upregulate host genes linked to anergy [29]. Schistosomiasis has also been associated with reduced autoimmunity, evidenced by lower antinuclear antibody (ANA) levels in individuals infected with *S. haematobium* [31]. Although schistosomiasis-induced immunity does not confer general protection against reinfection, elevated eosinophil levels have been identified as a likely protective factor in reinfection-resistant subpopulations [32]. Conversely, HIV coinfection correlates with increased reinfection rates, a phenomenon linked to blunted immune responses following praziquantel treatment [33]. While HIV does not completely abrogate the immune response to schistosomiasis, treated coinfecting individuals exhibit only an isolated increase in interleukin-5 (IL-5). In contrast, HIV-negative individuals demonstrate a robust, broad-spectrum response post-treatment, characterized by elevated levels of soluble worm antigen-specific IgG1–Ig4, IL-4, and IL-5 [33].

Given the complex interplay between HIV-induced immunosuppression and schistosomiasis-associated immune responses, we investigated the impact of HIV-related immune parameters on the reliability of antibody-based *Schistosoma* serodiagnosis. To this end, we screened for *Schistosoma* spp.-specific antibodies in sera of Ghanaian individuals with PCR-confirmed schistosomiasis—both with and without HIV coinfection—who presented without clinical signs of acute schistosomiasis or Katayama syndrome.

2. Materials and Methods

2.1. Sample Population

Residual serum samples with PCR-confirmed *Schistosoma* spp. DNA (deoxyribonucleic acid) [11,34] from Ghanaian individuals, both with and without HIV infection, were included in this assessment. As detailed elsewhere [34], these samples represent a subpopulation drawn from an original study of 1095 HIV-positive Ghanaian patients and a comparison group of 107 HIV-negative Ghanaian blood donors. While the presence of *Schistosoma* DNA was the primary inclusion criterion, samples were excluded if the residual

volume was insufficient for the serological testing described below. Clinical metadata available for the serum donors included age, sex, HIV status, and, for the HIV-positive cohort, immunological parameters from a previous assessment, specifically, CD4+ T-lymphocyte counts, CD4+/CD8+ ratios, and HIV viral loads [35,36]. Prior to further investigations, all serum samples had been stored deep-frozen at -80°C .

2.2. Serological Assessment

Anti-*Schistosoma* immunoglobulin G (IgG) and immunoglobulin M (IgM) were measured automatically using a commercial enzyme-linked immunosorbent assay (ELISA) provided by EUROIMMUN (EUROIMMUN Medizinische Labordiagnostika AG, Lübeck, Germany) on a EUROIMMUN Analyzer I device. Following the manufacturer's instructions for in vitro diagnostic use, the results were non-parametrically classified as positive, uncertain, or negative. Beyond the manufacturer's internal validation, independent diagnostic accuracy assessments have been published for this assay. A recent study in a Brazilian area endemic for *S. mansoni* reported a sensitivity of 100% and a specificity of 67% when evaluated against a composite reference standard of serological, microscopic, and molecular methods [37]. In our previous work assessing pregnant Madagascan women [38] with confirmed negative HIV status [39], the estimated sensitivity and specificity were 38.3% and 87.6% for the IgM assay, and 77.7% and 90.3% for the IgG assay, respectively. All samples included in the present study were tested in duplicate.

2.3. Interpretation of Serological Test Results and Statistical Analysis

Using the duplicate serological assessments, each sample was categorized into one of six ordinal groups for both anti-*Schistosoma* IgG and IgM reactivity: 0 = negative in both runs; 1 = uncertain in one run and negative in the other; 2 = uncertain in both runs; 3 = positive in one run and negative in the other; 4 = positive in one run and uncertain in the other; and 5 = positive in both runs. Category 5 was defined as "consistent", while all other profiles (categories 0–4) were classified as "inconsistent". Cycle threshold (Ct) values specific to either the *S. mansoni* or *S. haematobium* complex were obtained from prior analyses [34].

Categorical variables are presented as absolute frequencies and percentages, whereas continuous variables are summarized as medians with interquartile ranges (IQRs). Group comparisons between consistently positive participants (category 5) and those with inconsistent or negative profiles (categories 0–4) were performed using Fisher's exact test for categorical variables and the Mann–Whitney U test for continuous variables. To evaluate the relationship between host immune status and parasite burden, Spearman's rank correlation coefficient was calculated between CD4+ T-lymphocyte counts and PCR Ct values. Multivariable logistic regression models were constructed to identify independent factors associated with consistent IgG and IgM seroreactivity after adjusting for potential confounders. Adjusted odds ratios (aORs) and their corresponding 95% confidence intervals (CIs) are reported. Additional sensitivity analyses incorporated antiretroviral therapy status and HIV viral load. All statistical tests were two-tailed, and a p -value < 0.05 was considered statistically significant. Analyses were conducted using R software (version 4.5.3; R Foundation for Statistical Computing, Vienna, Austria).

2.4. Ethics

The samples were collected and analyzed in accordance with study protocols approved by the Committee on Human Research of the Kwame Nkrumah University of Science and Technology in Kumasi, Ghana (CHRPE/AP/12/11, approved on 8 September 2012), and the Ethics Committee of the Medical Council in Hamburg, Germany (PV3771). All study par-

ticipants provided written informed consent prior to enrollment. All procedures were conducted in full accordance with the Declaration of Helsinki and its subsequent amendments.

3. Results

3.1. Sample Characteristics

Following the application of the established case definitions and exclusion criteria, a total of 41 serum samples were included in the investigation. As detailed in Appendix A (Table A1), 36 samples tested positive for *S. mansoni* complex DNA, whereas 5 samples harbored *S. haematobium* complex DNA. Regarding serological profiling, detectable reactivity—ranging from borderline to strongly positive results—for anti-*Schistosoma* spp.-specific IgG or IgM was observed across all analyzed samples. Notably, none of the participants presented with clinical symptoms indicative of acute schistosomiasis or Katayama syndrome.

3.2. Characteristics of the Study Cohort

Of the 41 samples included in the study, 39 originated from HIV-positive individuals and two from HIV-negative participants. Within the HIV-positive cohort, qualitative PCR analysis revealed that the vast majority of *Schistosoma* infections were attributable to *S. mansoni* (92.3%, $n = 36$), while *S. haematobium* accounted for the remaining 7.7% ($n = 3$, Table 1). Conversely, only *S. haematobium* complex DNA was detected in the HIV-negative participants.

Table 1. Baseline demographic, clinical, and immunological characteristics of the HIV-positive study cohort, stratified by serological consistency regarding *Schistosoma*-specific IgM and IgG.

Parameter	Total HIV+ (N = 39)	IgG Inconsistent (N = 12)	IgG Consistent (N = 27)	p-Value	IgM Inconsistent (N = 8)	IgM Consistent (N = 31)	p-Value
Age (years), median [IQR]	35 (32–41.5)	33 (31.5–39.5)	36 (32–42.5)	0.464	35 (29.5–44.2)	35 (32–40.5)	0.820
Gender (female), n (%)	18 (46.2%)	4 (33.3%)	14 (51.9%)	0.470	5 (62.5%)	13 (41.9%)	0.521
Currently on ART, n (%)	13 (33.3%)	3 (25%)	10 (37%)	0.713	1 (12.5%)	12 (38.7%)	0.326
Piped water available, n (%)	17 (43.6%)	6 (50%)	11 (40.7%)	0.851	3 (37.5%)	14 (45.2%)	1.000
CD4+ T cells (/μL), median [IQR]	244 (60–391.8)	58 (31.5–78.5)	293 (137–427.5)	0.009	67.5 (42.2–136)	288.5 (83–442.8)	0.055
CD8+ T cells (/μL), median [IQR]	819 (433.5–1314.5)	306 (150–374)	981.5 (645.8–1375)	0.007	562 (258.5–1243.5)	838 (510.2–1349)	0.532
CD4/CD8 ratio, median [IQR]	0.2 (0.1–0.5)	0.1 (0.1–0.5)	0.3 (0.2–0.5)	0.564	0.2 (0.1–0.3)	0.3 (0.2–0.8)	0.153
HIV viral load (log10 copies/mL), median [IQR]	5 (3.1–5.5)	5 (3.2–5.7)	5 (2–5.5)	0.701	5.4 (4.1–5.5)	4.8 (2–5.7)	0.770
PCR Ct value, median [IQR]	31.6 (30.6–33.2)	32.4 (30.7–34)	31.4 (30.6–32.6)	0.267	31.3 (30.9–32.3)	31.6 (30.5–33.2)	0.986

ART, antiretroviral therapy; Ct, cycle threshold; IQR, interquartile range.

The median age of the HIV-positive sub-cohort was 35 years (IQR: 32–42), with females comprising 46.2% ($n = 18$) of the group. Antiretroviral therapy (ART) was actively utilized by 33.3% ($n = 13$) of these participants. The median CD4+ T-lymphocyte count was 244 cells/μL (IQR: 60–434), and the median HIV viral load was 5.0 log10 copies/mL (IQR: 3.1–5.5). Comprehensive baseline characteristics for this HIV-positive population are presented in Table 1.

3.3. Immunological and Clinical Parameters Stratified by Serological Consistency

Stratification of the cohort by IgG seroreactivity revealed significant immunological discrepancies between participants demonstrating consistently positive results across all serological test runs ($n = 27$) and those with inconsistent profiles ($n = 12$). Specifically, participants with consistent IgG positivity exhibited significantly higher median CD4+ T-lymphocyte counts compared to the inconsistent group (293 vs. 58 cells/μL, $p = 0.009$).

Correspondingly, CD8+ T-lymphocyte counts were also significantly elevated in the consistent IgG group (981.5 vs. 306 cells/ μ L, $p = 0.007$). Conversely, other parameters, including age, gender distribution, the CD4+/CD8+ T-lymphocyte ratio, HIV viral load, and PCR Ct values, demonstrated no statistically significant differences between the two IgG groups ($p > 0.05$ for all). When evaluating IgM serological consistency, individuals classified as consistently positive ($n = 31$) similarly demonstrated a trend toward higher median CD4+ T-lymphocyte counts than their counterparts with inconsistent or negative results ($n = 8$; 288.5 vs. 67.5 cells/ μ L); however, this variation approached but did not reach conventional statistical significance ($p = 0.055$).

3.4. Association Between Parasite Burden and Immune Status

To address potential confounding by infection intensity, specifically, the possibility that higher antibody consistency simply reflected a heavier parasite burden rather than host immune competence, we assessed the correlation between CD4+ T-lymphocyte counts and PCR Ct values. Spearman's rank correlation analysis revealed no significant relationship between host CD4+ T-lymphocyte counts and parasite Ct values ($\rho = 0.068$, $p = 0.686$).

3.5. Multivariable Determinants of Stable IgG and IgM Seropositivity

In a multivariable logistic regression model adjusted for PCR Ct value, age, and gender, higher CD4+ T-lymphocyte counts (scaled per 100 cells/ μ L) emerged as independent predictors of consistent IgG seropositivity (adjusted odds ratio [aOR] = 2.04, 95% CI: 1.25–4.00, $p = 0.013$, Figure 1). In contrast, PCR Ct values (aOR = 0.79, 95% CI: 0.49–1.14, $p = 0.237$), age, and gender demonstrated no significant independent associations with consistent IgG reactivity. Sensitivity analyses incorporating ART status or HIV viral load confirmed that the independent association between higher CD4+ T-lymphocyte counts and consistent IgG seroreactivity remained stable and robust. Similarly, multivariable adjustment for consistent IgM seropositivity revealed a parallel trend, with higher CD4+ T-lymphocyte counts showing a positive independent association that approached conventional significance (aOR = 1.74, 95% CI: 1.03–3.63, $p = 0.072$). Consistent with the IgG models, PCR Ct values (aOR = 0.94, 95% CI: 0.60–1.35, $p = 0.741$), age (aOR = 1.00, 95% CI: 0.86–1.17, $p = 0.963$), and gender (aOR = 0.70, 95% CI: 0.08–4.92, $p = 0.720$) exhibited no significant independent effects on stable IgM seroreactivity.

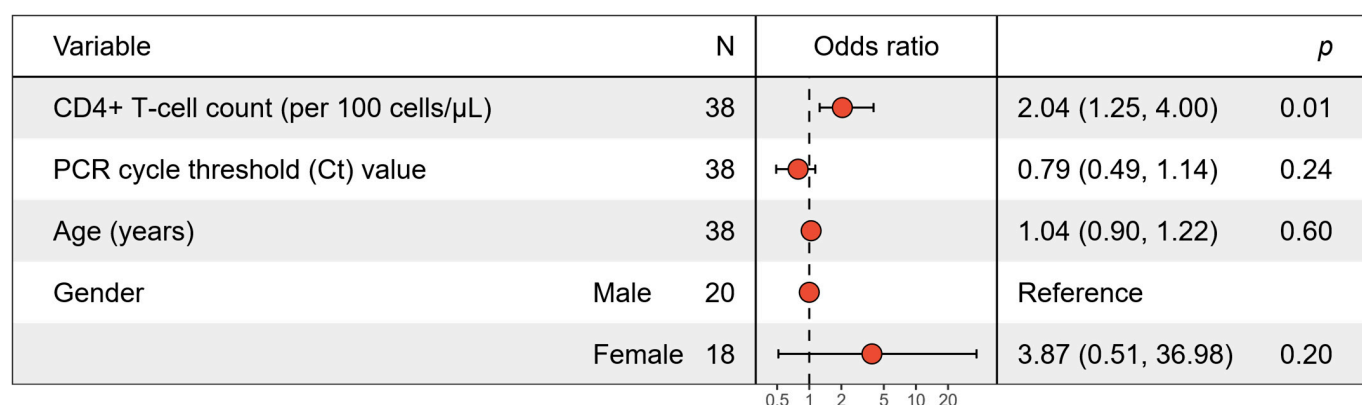


Figure 1. Forest plot displaying multivariable logistic regression analyses for factors associated with consistent *Schistosoma*-specific IgG seroreactivity. Adjusted odds ratios (aOR) and 95% confidence intervals (CI) are shown. Predictors include CD4+ T-lymphocyte counts (scaled per 100 cells/ μ L), PCR cycle threshold (Ct) values, age, and gender. One patient was excluded from multivariate analysis due to a missing CD4+ T lymphocyte count value.

4. Discussion

This study was conducted to assess the potential effects of HIV-associated immunosuppression on the reliability of the serodiagnosis of schistosomiasis. Both IgG and IgM antibodies were included in the assessment because the humoral responses to *Schistosoma* spp. egg and worm epitopes have been shown to be equivalent during both acute and chronic stages of the disease [40–42]. While HIV positivity is known to exert deleterious effects on the diagnostic sensitivity of serology for visceral leishmaniasis, another systemic parasitic infection [43], the potential impact of HIV-induced immunosuppression on *Schistosoma* serodiagnosis remains poorly addressed. This gap in the literature is particularly surprising given the extensive body of research demonstrating the complex immunological interactions between schistosomiasis and HIV infection [12–33].

Our assessment revealed a marked association between severely depleted cellular immunity and the inconsistent serological detection of anti-*Schistosoma* spp. antibodies in HIV-positive individuals. This phenomenon was more pronounced for the IgG subclass than for IgM. Because the medical histories of the assessed individuals did not suggest acute infections, considerable variability in anti-*Schistosoma* spp. IgM titers was not unexpected. Focusing specifically on CD4+ T-lymphocytes, the very low cell densities typical of late-presenting HIV infections [44] were strongly associated with inconsistent anti-*Schistosoma* IgG detection. Given that the START study has firmly established the benefits of early antiretroviral therapy [45], such severe AIDS-associated immune depletion should nowadays be the exception rather than the rule. Nevertheless, it remains a critical clinical consideration in settings where HIV diagnosis is delayed, for instance, due to fear of stigmatization [46].

The robustness of this association in multivariable testing strongly suggests that the observed serological inconsistency in the presence of severe cellular immunodeficiency is not merely coincidental. Notably, such a discrepancy between negative or inconsistent serology and positive PCR results requires careful consideration of both general assay limitations and factors associated with HIV infection. Data from a historical cohort of HIV-negative pregnant Madagascan women [38,39] assessed with identical assays showed that serological inconsistencies in immunocompetent individuals were strongly correlated with low parasite burdens, as evidenced by significantly higher *S. mansoni* PCR Ct values in the inconsistent IgG group compared to the consistent group (38.0 vs. 35.0; $p < 0.001$). In contrast, PCR Ct values were not associated with serological consistency in our HIV-positive cohort (aOR = 0.79, $p = 0.24$); rather, severe CD4+ T-cell depletion emerged as an independent correlate of diagnostic inconsistency. Furthermore, seropositivity in the absence of detectable *Schistosoma* DNA is a common finding in endemic areas, as serological assays cannot reliably differentiate between active infections and previous, therapeutically resolved schistosomiasis [8].

Hypothetically, very early *Schistosoma* spp. infections could also explain the detection of parasite DNA in the blood without concomitant seropositivity, given that anti-*Schistosoma* spp. DNA antibodies emerge relatively late in the course of infection [8,27]. However, neither the historical cohort of pregnant Madagascan women [38] nor the participants in the present study exhibited any clinical signs of Katayama syndrome or other indications of recent infection events. Therefore, while not formally excluded, a very early acute infection is highly unlikely to be the primary driver of the serological inconsistency observed here.

This study has several limitations. First, the retrospective design inherently restricts the analysis to the description of associations, precluding any definitive conclusions regarding causality or the potential recovery of serological consistency following ART-mediated immune reconstitution. Second, the modest sample size of PCR-positive individuals ($n = 41$) restricts statistical power and broadens the confidence intervals, increasing the

likelihood that associations with small to moderate effect sizes may have been overlooked. Third, because our investigation relied exclusively on a single commercial ELISA platform, the results may not fully generalize to assays utilizing alternative antigen preparations, such as soluble egg antigen versus adult worm antigen [8]. Finally, due to the absence of multiple testing corrections, this study is strictly exploratory and hypothesis-generating in nature [47]. Consequently, all reported *p*-values should be interpreted with appropriate caution.

5. Conclusions

Despite these limitations, this study highlights the vulnerability of serology-based schistosomiasis diagnostics to severe cellular immune depletion in HIV-positive patients. Consequently, negative or inconsistent anti-*Schistosoma* spp. antibody results must be interpreted with caution in this population, particularly when there is a strong clinical or epidemiological suspicion of schistosomiasis. In such cases of advanced immunosuppression, clinicians should strongly consider alternative diagnostic approaches, such as highly sensitive real-time PCR assays [11], to ensure accurate detection and appropriate patient management.

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Institutional Review Board Statement: The included samples were collected and analyzed in line with the protocols approved by the Committee on Human Research of the Kwame Nkrumah University of Science and Technology in Kumasi, Ghana: CHRPE/AP/12/11 (approved on 8 September 2012), as well as by the ethics committee of the Medical Council in Hamburg, Germany: PV3771 (13 May 2011). The respective study participants provided written informed consent prior to enrolment. All assessments were performed in full accordance with the Declaration of Helsinki and all its amendments.

Informed Consent Statement: All study participants provided written informed consent prior to enrolment.

Data Availability Statement: All relevant data are presented either in the manuscript text or its appendix tables.

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Abbreviations

The following abbreviations are used in this manuscript:

ADCC	antibody-dependent cellular cytotoxicity
AIDS	acquired immunodeficiency syndrome
ANA	antinuclear antibodies
aOR	adjusted odds ratio
ART	anti-retroviral therapy
CI	confidence interval
DNA	deoxyribonucleic acid
ELISA	enzyme-linked immuno-sorbent assay
env	Envelope
HIV	human immunodeficiency virus
Ig	immune globulin
IQR	inter-quartile range
IRIS	immune reconstitution inflammatory syndrome
vif	virion infectivity factor
PCR	polymerase chain reaction
Th	T-helper

Appendix A

Table A1. Cycle threshold values of *Schistosoma mansoni* complex-specific as well as *Schistosoma haematobium* complex-specific real-time PCR as well as qualitative results of automated anti-*Schistosoma* spp.-IgG-specific and anti-*Schistosoma* spp.-IgM-specific serological testing. Serological results were obtained in duplicate and non-parametrically assigned as follows: 0 = negative in both runs, 1 = uncertain in one run, negative in the other one, 2 = uncertain in both runs, 3 = positive in one run, negative in the other one, 4 = positive in one run, uncertain in the other one, 5 = positive in both runs. Categories 0–4 were defined as “inconsistent”, category 5 as “consistent”.

Fully Anonymized Sample Number	Cycle Threshold Value of <i>S. mansoni</i> Complex-Specific Real-Time PCR (<i>Sm1–7</i> Sequence)	Cycle Threshold Value of <i>S. haematobium</i> Complex-Specific Real-Time PCR (<i>Dra1</i> Sequence)	Qualitative Results of Automated Anti- <i>Schistosoma</i> spp.-IgG-Specific Serology	Qualitative Results of Automated Anti- <i>Schistosoma</i> spp.-IgM-Specific Serology
1	33.5	-	5 (consistent)	1 (inconsistent)
2	30.8	-	5 (consistent)	4 (inconsistent)
3	30.4	-	5 (consistent)	5 (consistent)
4	28.8	-	5 (consistent)	5 (consistent)
5	28.8	-	5 (consistent)	5 (consistent)
6	33.1	-	5 (consistent)	5 (consistent)
7	31.6	-	5 (consistent)	5 (consistent)
8	24.1	-	5 (consistent)	5 (consistent)
9	32.0	-	5 (consistent)	5 (consistent)
10	33.8	-	2 (inconsistent)	5 (consistent)
11	31.8	-	5 (consistent)	5 (consistent)
12	31.6	-	5 (consistent)	5 (consistent)
13	28.4	-	5 (consistent)	5 (consistent)
14	31.5	-	5 (consistent)	5 (consistent)
15	30.5	-	5 (consistent)	5 (consistent)
16	31.0	-	5 (consistent)	4 (inconsistent)
17	33.3	-	5 (consistent)	5 (consistent)
18	30.0	-	2 (inconsistent)	4 (inconsistent)
19	34.1	-	4 (inconsistent)	5 (consistent)
20	31.1	-	5 (consistent)	5 (consistent)
21	31.1	-	5 (consistent)	5 (consistent)
22	30.6	-	5 (consistent)	5 (consistent)

Table A1. Cont.

Fully Anonymized Sample Number	Cycle Threshold Value of <i>S. mansoni</i> Complex-Specific Real-Time PCR (<i>Sm1–7</i> Sequence)	Cycle Threshold Value of <i>S. haematobium</i> Complex-Specific Real-Time PCR (<i>Dra1</i> Sequence)	Qualitative Results of Automated Anti- <i>Schistosoma</i> spp.-IgG-Specific Serology	Qualitative Results of Automated Anti- <i>Schistosoma</i> spp.-IgM-Specific Serology
23	32.3	-	5 (consistent)	5 (consistent)
24	31.4	-	5 (consistent)	0 (inconsistent)
25	31.8	-	5 (consistent)	5 (consistent)
26	30.5	-	5 (consistent)	5 (consistent)
27	32.9	-	5 (consistent)	5 (consistent)
28	35.7	-	5 (consistent)	5 (consistent)
29	34.3	-	5 (consistent)	5 (consistent)
30	34.5	-	2 (inconsistent)	0 (inconsistent)
31	33.2	-	5 (consistent)	5 (consistent)
32	30.0	-	2 (inconsistent)	5 (consistent)
33	32.9	-	2 (inconsistent)	5 (consistent)
34	30.9	-	0 (inconsistent)	5 (consistent)
35	29.4	-	0 (inconsistent)	5 (consistent)
36	35.5	-	0 (inconsistent)	5 (consistent)
37	-	30.1	5 (consistent)	5 (consistent)
38	-	30.9	1 (inconsistent)	5 (consistent)
39	-	34.0	0 (inconsistent)	5 (consistent)
40	-	31.9	4 (inconsistent)	0 (inconsistent)
41	-	31.2	1 (inconsistent)	4 (inconsistent)

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