# Schistosoma mansoni coinfection is associated with high Plasmodium falciparum infection intensity among 10 -15 year old children living along the Albert Nile in Uganda

**Joyce Namulondo**
Makerere University
**Oscar Asanya Nyangiri**
Makerere University
**Magambo Phillip Kimuda**
Makerere University
**Peter Nambala**
Makerere University
**Jacent Nassuuna**
MRC/UVRI and LSHTM Uganda Research Unit
**Joyce Kabagenyi**
MRC/UVRI and LSHTM Uganda Research Unit
**Moses Egesa**
MRC/UVRI and LSHTM Uganda Research Unit
**Barbara Nerima**
Makerere University
**Savino Biryomumaisho**
Makerere University
**Claire Mack Mugasa**
Makerere University
**Alison Elliott**
MRC/UVRI and LSHTM Uganda Research Unit
**Harry Noyes**
University of Liverpool
**Robert Tweyongyere**
Makerere University
**Enock Matovu**
Makerere University

**Julius Mulindwa**

julius.mulindwa@mak.ac.ug

Makerere University

**Research Article**

**Keywords:** Plasmodium, falciparum, Schistosoma, mansoni, association

**Posted Date:** May 2nd, 2024

**DOI:** https://doi.org/10.21203/rs.3.rs-4318753/v1



**Additional Declarations:** No competing interests reported.

## Abstract

# Background

Malaria and schistosomiasis are important parasitic diseases. Coinfections of these have been reported in areas endemic to both parasites. The aim of this study was to determine the association between *Schistosoma mansoni (S. mansoni)* and *Plasmodium falciparum (P. falciparum)* infection intensities among school age children living along the Albert Nile.

# Methods

A cross sectional study of 210 children aged 10–15 years, was conducted in selected sites along the Albert Nile in Pakwach District in northwest Uganda. The Circulating Anodic Antigen (CAA) test and quantitative PCR (qPCR) were used to test for *S. mansoni* infection intensity and quantitative PCR used to test for *P. falciparum* infection intensity.

# Results

Of the 210 study particpants, 76.2% (160/210) were malaria positive whereas 91% (191/210) were *S. mansoni* positive. There were only 1% (3/210) infections of each of *Necator americanus* and *Strongyloides stercolaris*. Of the *P. falciparum* positive children 57.5% (92/160) were male; on the other hand 53.4% (102/191) of the *S. mansoni* positive children were male. Overall, 150 of the 210 children tested (71%) had co-infection with both *P. falciparum* and *S. mansoni*. There was a significant association (p-value = 7.306e-10, $r^2$ = 0.17) between *P. falciparum* qPCR Ct-value and *S. mansoni* qPCR Ct-value. There was a significant association (p-value = 7.306e-10, $r^2$ = 0.17) between *P. falciparum* intensity (qPCR Ct-value) and *S. mansoni* intensity *(*qPCR Ct-value) among the children test.

# Conclusions

By molecular detection, this study observed a high prevalence of *P. falciparum* among the school age children (10–15 years) living in the *S. mansoni* endemic hotspots along the Albert-Nile region of Pakwach district, northwestern Uganda.


## Summary

Schistosomiasis and malaria are important parasitic diseases endemic in Uganda. The predominant schistosomiasis causing species in Uganda is *Schistosoma mansoni* while that for malaria is *Plasmodium falciparum*. Coinfections occur in areas with high endemicity of these two parasites. *S. mansoni* coinfection has previously been shown to alter the clinical presentation of malaria. In this study,

we used quantitative PCR (qPCR) to determine the association between *P. falciparum* infection and *S. mansoni* infection intensities. We observed high *P. falciparum* infection intensities in areas closer to the Albert Nile compared to those farther away. We recorded 71.4% coinfections with *P. falciparum* and *S. mansoni* using qPCR for the two parasites. Our data showed an association between *P. falciparum* and *S. mansoni* infection in children between 10 -15 years living along the Albert Nile; there was increased *S. mansoni* infection intensity among children with high *P. falciparum* infection intensity.

# Background

Schistosomiasis and malaria are important parasitic diseases that cause morbidity and mortality worldwide [1–3]. Schistosomiasis is widespread in tropical and sub-tropical regions with over 78 countries reporting transmission [4]. The World Health Organization (WHO) estimated that 236.6 million people required treatment for schistosomiasis in 2019 [5]. Additionally, WHO estimated 249 million malaria cases in the endemic areas [3]. Malaria and schistosomiasis coinfection has been reported in areas with high occurrence of both infections [6–8]. Additionally stunting among children has been shown in *S. mansoni* as well as *P. falciparum*[9] infection Coinfection of malaria and schistosomiasis is particularly common in sub Saharan Africa (SSA) [10].

Despite control measures such as use of mosquito nets or Indoor Residual Spraying (IRS), Uganda has the third highest malaria incidence after Nigeria and the Democratic Republic of Congo [3] in Africa. In Uganda, malaria is predominantly caused by *Plasmodium falciparum* and infections are transmitted throughout the year [11]. High prevalence of malaria has been reported around Lake Albert [12]. A recent study showed a reduction in stunting following treatment of malaria infection[13].

Uganda is also endemic for schistosomiasis with varying prevalence in different localities. Our recent survey showed high prevalence of schistosomiasis caused by *S. mansoni* in children of school age from villages along the Albert Nile with high levels of stunting which were not associated with schistosomiasis [14]. This adds to previous findings on high prevalence of *S. mansoni* by Lake Albert [15, 16].

*S. mansoni* coinfections with *Plasmodium* species are known to influence clinical presentation of malaria[8, 17, 18] and may also alter the immune response to infection and affect response to treatment and vaccination [19]. Individuals with *P. falciparum / S. mansoni* coinfections are reportedly more prone to frequent and severe malaria [20]. This study aimed to determine the prevalence of circulating *P. falciparum* in *S. mansoni* infected school age children and the association of *P. falciparum* with *S. mansoni* infection intensity in the schistosomiasis hotspots of the Albert Nile in Uganda as well as association of *P. falciparum* with stunting among the school age children (10–15 years).

# Methods

# Study design and study sites

This was a cross-sectional study that was carried out in communities along the Albert Nile in Pakwach District in North Western Uganda. Blood and fecal samples were collected from school children aged between 10–15 years. The selected sampling sites were in four (4) sub-counties of Pakwach, Panyingoro, Panyimur and Alwi all with close visinity to the Albert Nile.

# Screening and sample collection

The point of care cathodic circulating antigen (POC-CCA) (Rapid Medical Diagnostics, Pretoria, South Africa, batch No. 191031120) was used in the field for screening for *S. mansoni* and classifying participants by infection intensity to select and collect blood samples that were tested for *P. falciparum* and *S. mansoni* by quantitative PCR (qPCR) as previously described [14, 21]. Following the interview, each selected participant was requested to provide stool in stool containers and peripheral blood in EDTA tubes (BD Biosciences, US) for plasma separation. Briefly, to obtain the plasma, 4 ml of venous collected in an EDTA tube was centrifuged at 5000 rpm to separate the sample into packed cells and plasma. The plasma was temporarily stored in liquid nitrogen while in the field and transfered to -80$^0$C freezer in the central laboratory for quantification of schistosome infection intensity by the Circulating Anodic Antigen (CAA) test. The packed cells were lysed using Red Blood Cell (RBC) lysis solution (Qiagen) and the remaining nucleated cells stored in liquid nitrogen for *P. falciparum* infection testing by qPCR. Additionally stool sample portions were stored in liquid nitrogen to conduct qPCR for other helminths and *S. mansoni* in the laboratory.

### Circulating Anodic Antigen (CAA) assay for S. mansoni infection

To classify infection intensity, CAA levels were measured in plasma using the up-converting phosphor lateral flow-circulating anodic antigen (UCP-LF CAA) assay [22]. A standard curve was generated using human negative serum spiked with a known concentration of CAA standard (100,000 pg/ml) and diluted up to eight standard points, with two negative controls. Briefly, 50 µl of each of the plasma and standards was mixed with 50 µl of 4% trichloroacetic acid (TCA; Merck Life Science NV, the Netherlands),vortexed and incubated for 5 minutes at room temperature. Following centrifugation at 13000rpm for 5 minutes, 20µl of the supernatant was incubated in the wells containing 100 ng dry UCP particles (400 nm Y2O2S: Yb3+, Er3+) coated with mouse monoclonal anti-CAA antibodies hydrated with 100µl of high salt lateral flow buffer (HSLF: 200 mM Tris pH8, 270 mM NaCl, 0.5% (v/v) Tween-20, 1% (w/v) BSA) for 1 hour at 37$^0$C while shaking at 900 rpm. Pre-labelled CAA lateral flow strips were placed in the wells on the UCP plate and allowed to flow. The strips were left to dry overnight and quantified using the Labrox Upcon scanner (Labrox Oy, Finland) from which CAA concentrations were calculated in pg/ml. The test line signals (T; relative fluorescent units, peak area) were normalized to the flow control signals (FC) of the individual strips and the results were expressed as ratio values. CAA concentrations > 30 pg/mL were classified as positive; negative (CAA < 30 pg/mL). Additionally, CAA levels from 30–1000 pg/mL were classified as low infection intensity and CAA > 1000 pg/mL as high infection intensity as adapted from Corstjens et al [23] and with advice from the assay development team at the Leiden University Medical Centre, The Netherlands (Leiden Diagnostic Research Group | LUMC).

### Plasmodium falciparum detection

To determine *P. falciparum* presence, DNA was extracted from whole blood pellets using the QIAamp DNA Blood Mini Kit (Catalogue number 51106, QIAGEN) following the manufacturer's manual. The real-time PCR was performed with the ABI 7500 Fast Real-time machine and data processed using 7500 Fast Systems software version 1.5.1. A final volume of 25 µl containing 2 µl of DNA 1 µl of PhHV DNA (internal control) and 22 µl of PCR master mix made of HotStarTaq Master Mix (Catalogue Number 203446), primers, and probes was added (**Table S1**). A pool of DNA extracted from *P. falciparum* positive samples was used to set serially diluted standards tested alongside the samples on every plate run. The following cycling parameters were used; 95°C for 15 min; 95°C for 15 sec; 60°C for 30 sec; and 72°C for 300 sec, steps 3–5 repeated 50 times.

## Helminth detection

Frozen stool samples were used for detecting helminths in stool by qPCR. Briefly, helminth DNA was extracted from stool using the Fast DNA Spin Kit for Feces (catalogue number 116570200, MP Biomedicals Germany GmbH) to determine (using multiplex real-time PCR) *Schistosoma mansoni* (*S. mansoni*), *Strongyloides stercoralis* (*S. stercoralis*) and *Necator americanus* (*N. americanus*) infections. The real-time PCR was performed with the ABI 7500 Fast Real-time machine and data processed using 7500 Fast Systems software version 1.5.1. A final volume of 25 µl containing 2 µl of DNA 1 µl of PhHV DNA (internal control) and 22 µl of PCR master mix made of HotStarTaq Master Mix (Catalogue Number 203446), primers, and probes was added (**Table S1**). A pool of DNA extracted from *P. falciparum* positive samples was used to set serially diluted standards tested alongside the samples on every plate run. The following cycling parameters were used; 95°C for 15 min; 95°C for 15 sec; 60°C for 30 sec; and 72°C for 300 sec, steps 3–5 repeated 50 times.

## Statistical analysis

Data analysis was done in R software version 4.22. For all the parasites tested, qPCR cycle threshold values ( Ct-values ) above 40 were classified as negative. PCR Ct-values are inversely proportional to infection intensity i.e; individuals with low Ct-value had higher infection intensity and those with high Ct-values had low infection intensity. Pearson's correlation test and linear regression analysis were used to determine association between *S. mansoni* qPCR and CAA, *P. falciparum* infection and CAA, *P. falciparum* infection and *S. mansoni* qPCR as well as *P. falciparum* infection and height by age z-scores. The Fisher exact test was done to establish whether the coinfections were more or fewer than expected by chance.

## Results

A total of 210 children had samples matched with stool and CAA results of which 98 were female and 112 were males **(**Table 1**).** Of the total, 76.2% (160 /210) were *P. falciparum* positive whereas 91% (191/210) were *S. mansoni* positive as detected by quantitative PCR (qPCR). Only 1% (3/210) of participants had infections with each of *Necator americanus* and *Strongyloides stercolaris* were

detected. Of the *P. falciparum* positive participants 42.5% (68/160) were female and 57.5% (92/160) were male. The difference in *P. falciparum* prevalence in males and females was significant with a Chi-squared p-value of 0.04 (Fig. 1A **&B**). Of the *S. mansoni* positive, 46.6% (89/191) were female and 53.4% (102/191) were male but the differences in prevalence were not significant. Nyakagei had the highest *P.falciparum* 92% (69/75) and *S. mansoni* 95% (71/75) infections. Alwi had the least infections with both *P. falciparum* 8% (1/12) and *S. mansoni* 33% (4/12) (Fig. 2**)**.

Table 1
Summary of parasitic infections by gender. Of the 210 individuals tested, 160(76%) were infected by *P.falciparum*, 191(91%) with *S. mansoni*. There were very few *N. americanus* and *S. stercolaris* infections among these children.

| | Female | Male | Total | %positivity |
|---|---|---|---|---|
| **Total** | 98 | 112 | 210 | |
| **P. falciparum** | 68 | 92 | 160 | 76% |
| **S. mansoni** | 89 | 102 | 191 | 91% |
| **N. americanus** | 1 | 2 | 3 | 1% |
| **S. stercolaris** | 0 | 3 | 3 | 1% |

# Parasitic coinfections

Of the 210 children tested, 150 (71%) had concomitant infection with *P. falciparum* and *S. mansoni* with slightly less coinfections than expected by chance (Fisher exact test p-value of 0.02) (Table 2). There were no coinfections with only *S. mansoni* or only *P. falciparum* with *Necator americanus* or *Strongyloides stercolaris*. Only 2 (1%) of the total tested samples had a triple coinfection with *P. falciparum*, *S. mansoni* and *N. americanus* and 2 (1%) had triple coinfections with *P. falciparum*, *S. mansoni* and *S. stercolaris*. There were no duo coinfections of *S. mansoni* and *Necator americanus* or *Strongyloides stercolaris*. Only 2 (1%) of the total tested had a triple coinfection with *P. falciparum*, *S. mansoni* and *N. americanus* and 2(1%) had triple coinfections with *P. falciparum*, *S. mansoni* and *S. stercolaris*.

Table 2

**A summary of P. falciparum and S. mansoni infections by PCR (negative, mono and coinfections)**: There were 71% (150/210) concurrent infections with both *P. falciparum* and *S. mansoni* which was slightly less than the expected 69% (145.5/210) by chance (p-value = 0.02).

| **Exact values** | | | | **Expected values** | |
|---|---|---|---|---|---|
| Pathogen | | **P. falciparum** | | | |
| **S. mansoni** | | Negative | Positive | Negative | Positive |
| | Negative | 9 | 41 | 4.5 | 45.5 |
| | Positive | 10 | 150 | 14.5 | 145.5 |

### Association between PCR and CAA tests for S. mansoni

Pearson's correlation test and regression analysis were used to compare the *S. mansoni* qPCR Ct-values with the *S. mansoni* CAA values. There was a significant negative association (p-value = 3.2e-16, $r^2$ = -0.27) between *S. mansoni* PCR Ct-values and CAA **(**Fig. 3**).** The negative correlation is due to the fact that lower qPCR Ct-values are indicative of high infection intensity contrary to CAA for which higher values indicate high infection intensity.

### Association between P. falciparum infection and S. mansoni infection

Pearson's correlation test and regression analysis were used to compare the *P. falciparum* PCR Ct-values with the *S. mansoni* CAA and qPCR Ct-values. There was a significant negative association (p-value = 7.3e-10, $r^2$ = -0.17) between *P. falciparum* infection and *S. mansoni* CAA **(**Fig. 4A**)** and a significant positive association (p-value = 2.9e-06, $r^2$ = 0.10) between *P. falciparum* and *S. mansoni* infection intensity by PCR (Fig. 4B). We further conducted a linear regression to interrogate the association between *P. falciparum* as well as *S. mansoni* with age, sex and sites (Table 3).

Table 3
Linear regression model *P. falciparum* PCR vs *S. mansoni* CAA

| | Estimate | Std. Error | t value | pvalue | Odds Ratio |
|---|---|---|---|---|---|
| log(CAA) | -0.52 | 0.16 | -3.351 | 0.000961 *** | 0.59 |
| Age | 0.42 | 0.23 | 1.848 | 0.06 . | 1.52 |
| Sex | -1.47 | 0.73 | -2.013 | 0.04 * | 0.23 |
| Alwi | 5.64 | 1.99 | 2.831 | 0.005 ** | 282 |
| Dei | 2.54 | 1.19 | 2.130 | 0.03 * | 12.6 |
| Kayonga | 0.46 | 1.09 | 0.424 | 0.67 | 1.58 |
| Kivuje | 2.96 | 1.15 | 2.561 | 0.01 * | 19.2 |
| Panyigoro | 2.27 | 1.28 | 1.774 | 0.07 | 9.69 |
| Significance. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1, Residual standard error: 5.135 on 201 degrees of freedom (DF), Multiple R-squared: 0.2564, Adjusted R-squared: 0.2268, F-statistic: 8.663 on 8 and 201 DF, p-value: 3.881e-10 | | | | | |

### Association between P. falciparum infection and Stunting

The Pearson's correlation test and regression analysis were used to compare the *P. falciparum* PCR Ct-values with height-for-age z-scores obtained using the WHO 2007 reference to determine if there was an association between *P. falciparum* Ct-values and stunting, [25]. We defined stunting as HAZ <-2 standard deviations (SDs). There was no association between malaria infection and HAZ (p-value = 0.48).

### Distribution of P. falciparum and S. mansoni infection intensity by location

We used PCR Ct-values to identify the distribution of *P. falciparum* and *S. mansoni* infection intensity by site (Fig. 2). Alwi, which was furthest from the Albert Nile had the lowest *P. falciparum* and *S. mansoni* prevalence and infection intensities measured by the mean qPCR Ct-values. Areas closer to the Albert Nile [14] had a higher infection intensity of both *P. falciparum* and *S. mansoni* compared to those further away. Nyakagei had infections with highest intensity for *P. falciparum* as well as *S. mansoni* based on the mean Ct-value, followed sequentially by Kayonga, Dei, Kivuje and Panyigoro.

## Discussion

Parasitic coinfections have been reported in several studies, as recently reviewed [8], among which are *P. falciparum* and *S. mansoni* coinfection [6–8]. In this study, we present findings of a cross-sectional analysis set out to ascertain the association between *S. mansoni* infection and *P. falciparum* infection.

We used both CAA and PCR to estimate *S. mansoni* infection intensity. Our data shows an association between real-time PCR and CAA as tests for *S. mansoni* detection. Our model however, showed a weak

negative correlation between the two methods of detection of *S. mansoni* with an $r^2$ value − 0.27. The negative correlation is due to the fact that lower qPCR Ct-values are indicative of high infection intensity contrary to CAA for which higher values indicate high infection intensity.

Our findings add to previous studies that indicated PCR as a better indicator for *S. mansoni* infection intensity than the Kato Katz assay and can be used without microscopic examination of stools for parasite eggs [26, 27] although less sensitive than CAA [27]. PCR is a more sensitive method of *P. falciparum* detection compared to microscopy especially at low intensity [28, 29]. In this study we recorded 76.2% *P. falciparum* and 91% *S. mansoni* infections among the 210 children tested. The frequency of *P. falciparum* infections was higher in males compared to females with Chi-squared p-value of 0.04. This may be attributed to a variety of factors including lifestyle as previously shown [11, 30, 31].

Our study area has a high prevalence of *S. mansoni*[14] as well as high *P. falciparum* transmission [32]. We observed high *P. falciparum* infection intensities in areas closer to the Albert Nile than those further away which may indicate high vector infestation in proximity to the Nile. Coinfection of *P. falciparum* and *S. mansoni* is common in areas where both parasites are endemic. In this study, we recorded 71.4% coinfections with *P. falciparum* and *S. mansoni* using PCR for the two parasites. Previous findings in Ethiopia showed that individuals with high *S. mansoni* intensity had high *P. falciparum* intensity[17] contrary to previous findings among pre-school children in Uganda [33]. Our data showed a weak association between *P. falciparum* and *S. mansoni* infection intensity in children between 10–15 years living along the Albert Nile with an absolute $r^2$ 0.1–0.17 by Pearson's correlation coefficient. Individuals with high *P. falciparum* infection intensity also tended to have high *S. mansoni* infection intensity. In Ethiopia, the 6–10 age group was reportedly more prone to severe malaria if coinfected with *S. mansoni* [17]. Whether the intensity is due to shared risk of proximity to the Albert Nile or pathogen factors within the parasites was not established in our study. Coinfections have been shown to alter susceptibility to pathogens hence altering the immune activity[34] and further affecting diagnosis which may lead to prolonged disease [8].

Coinfections have been shown to affect susceptibility to pathogens hence altering the immune activity [34] and further affecting diagnosis which may lead to prolonged disease [8]. Animal studies have shown that coinfection with *S. mansoni* is associated with an increase in *Plasmodium* parasitemia but reduced *S. mansoni* induced pathology [35]. Recent studies have reported increased risk of anaemia in individuals with both malaria and *S. mansoni* [6]. In our previous study, we observed high levels of stunting amongst participants but this had no association with *S. mansoni* infection. We also observed no association between *P. falciparum* infection and stunting contrary to previous studies [36].

The major limitation of or study was that malaria clinical and microscopy data were not recorded and therefore any association between coinfection and disease severity cannot be estimated.

# Conclusions

In conclusion, our study shows a high prevalence of *P. falciparum* and *S. mansoni* infection among 10–15 year old children living along the lake Albert. The data show concurrent infection with both *P. falciparum* and *S. mansoni* among these children. Furthermore, there was an association between *P. falciparum* Ct-values and *S. mansoni* infection intensity. We show that individuals with high malaria parasitemia had high *S. mansoni* infection intensity. Joint surveillance and intervention programmes are required to better understand and control the *P. falciparum* and *S. mansoni* infection and to inform policy makers on combined drug administration by the National control programme.

# Declarations


### Acknowledgement

We acknowledge and thank all the children and the parents/guardians that participated in this study. We appreciate Vector Control Division (VCD) and the efforts by the Village health team members and the local council administrators of the villages of Panyigoro, Kivuje, Nyakagei, Kayonga, Dei, and Alwi. The Membership of the TrypanoGEN+ Research group of the H3Africa Consortium: Annette MacLeod, Bruno Bucheton, Gustave Simo, Dieudonne N. Mumba, Mathurin Koffi, Ozlem T. Bishop, Pius V. Alibu, Janelisa Musaya, and Christiane Hertz-Fowler

### Funding Information

This work was supported by Human Heredity and Health in Africa (H3Africa) [H3A-18-004]. H3Africa is managed by the Science for Africa Foundation (SFA Foundation) in partnership with Wellcome, NIH and AfSHG. The views expressed herein are those of the author(s) and not necessarily those of the SFA Foundation and her partners.


### Availability of data and materials

All relevant data are contained within the manuscript.

### Author contributions

**Joyce Namulondo**: Conceptualization, Methodology, Investigation, Administration, Formal analysis, Writing – Original Draft preparation; **Oscar Nyangiri:** Formal analysis, Writing – review & editing; **Magambo Phillip Kimuda**: review & editing; **Peter Nambala**: Formal analysis, Writing – review & editing; **Jacent Nassuuna:** Writing – review & editing**, Alison Elliott:** Resources Writing – review & editing; **Moses Egesa:** Writing – review & editing; **Joyce Kabagenyi:** Writing – review & editing; **Barbara Nerima**: review & editing; **Savino Biryomumaisho**: review & editing; **Claire Mack Mugasa:** review & editing; **Harry Noyes:** Investigation, Supervision, Formal analysis, Writing – review & editing; **Robert Tweyongyere:** review & editing; **Enock Matovu:** Investigation, Supervision, Resources, Writing – review & editing; **Julius Mulindwa**: Conceptualization, Methodology, Investigation, Supervision, Formal analysis, Writing – review & editing.

### Ethics statement

The study protocol was reviewed by the institutional review board of the Ministry of Health, Vector Control Division Research and Ethics Committee (Reference No. VCDREC106) and approved by the Uganda National Council for Science and Technology (Reference No. UNCST HS 118). The study was conducted with guidance from the district health officials, including the selection and training of the village health teams that were involved in the mobilisation and recruitment of the children (10 -15 years) into the study. The objectives, potential risks and benefits of the study were explained to the parents/guardians, who signed written informed consent. The same was later explained to the school age children in English and Alur dialect before they provided written assent for participation in the study. If a child was observed to have *S. mansoni* eggs in their stool, they were offered free treatment, which consisted of praziquantel at a dosage of 40mg/kg administered by trained Ministry of Health personnel, assisted by district health workers. Point of care cathodic circulating antigen (POC-CCA) and *P. falciparum* results were not used as an indication for treatment.

Consent for publication

Not applicable.

Competing details

The authors declare no conflict of interests.

# References


1. LoVerde PT. Schistosomiasis. Adv Exp Med Biol. 2019;1154:45–70.
2. McManus DP, Dunne DW, Sacko M, Utzinger J, Vennervald BJ, Zhou XN, et al. Schistosomiasis. Nat Rev Dis Primers. 2018;4:13.
3. World malaria report 2023. https://www.who.int/publications/i/item/9789240086173. Accessed 31 Jan 2024.
4. Colley DG, Bustinduy AL, Secor WE, King CH. Human schistosomiasis. Lancet. 2014;383:2253.
5. WHO. Schistosomiasis and soil-transmitted helminthiases: numbers of people treated in 2019 – Schistosomiase et géohelminthiases: nombre de personnes traitées en 2019. Weekly Epidemiological Record = Relevé épidémiologique hebdomadaire. 2020;95:629–40.
6. Dassah SD, Nyaah KE, Senoo DKJ, Ziem JB, Aniweh Y, Amenga-Etego L, et al. Co-infection of *Plasmodium falciparum* and *Schistosoma mansoni* is associated with anaemia. Malar J. 2023;22:1–15.
7. Kamau E, Yates A, Maisiba R, Singoei V, Opot B, Adeny R, et al. Epidemiological and clinical implications of asymptomatic malaria and schistosomiasis co-infections in a rural community in western Kenya. 2021. https://doi.org/10.1186/s12879-021-06626-2.

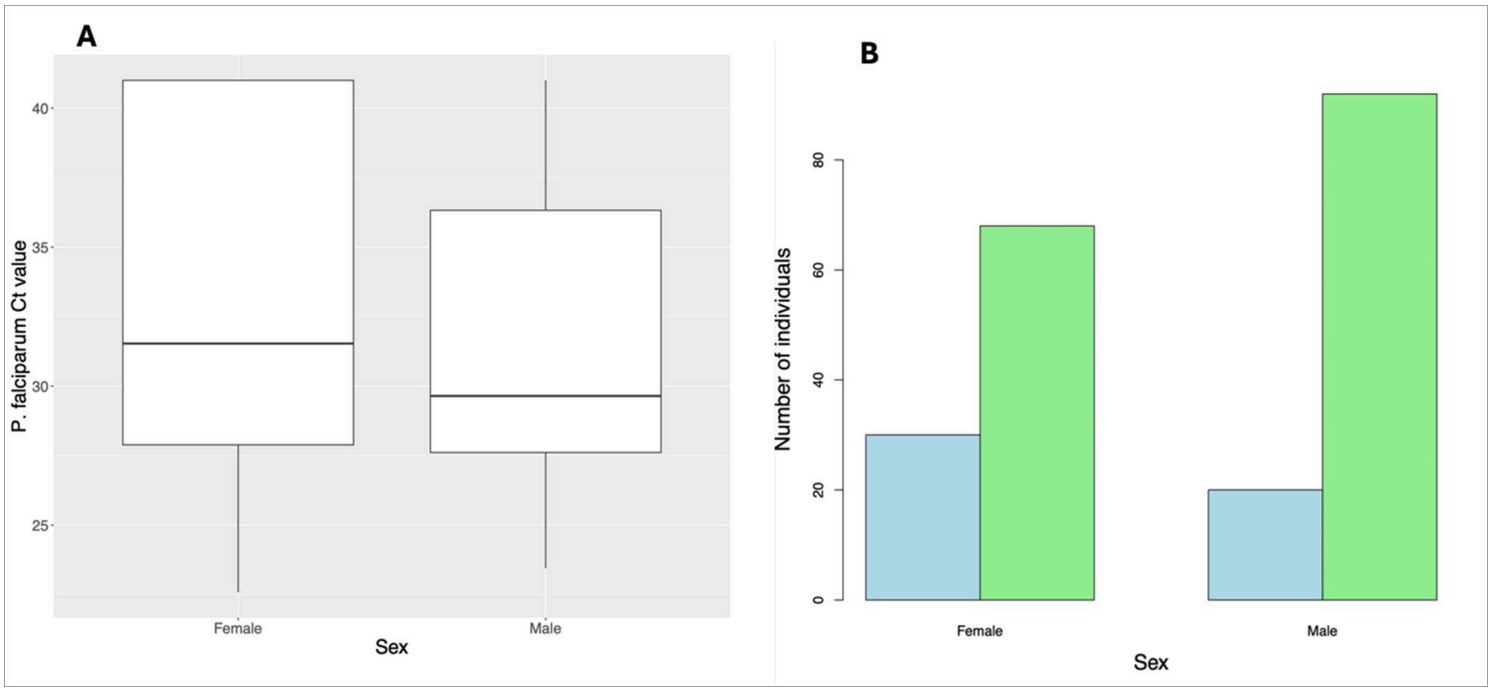
8. Hananeh WM, Radhi A, Mukbel RM, Ismail ZB. Effects of parasites coinfection with other pathogens on animal host: A literature review. 2022. https://doi.org/10.14202/vetworld.2022.2414-2424.
9. Gebreegziabher E, Dah C, Coulibaly B, Sie A, Bountogo M, Ouattara M, et al. The Association between Malnutrition and Malaria Infection in Children under 5 Years in Burkina Faso: A Longitudinal Study. Am J Trop Med Hyg. 2023;108:561–8.
10. Brooker S, Akhwale W, Pullan R, Estambale B, Clarke SE, Snow RW, et al. Epidemiology of plasmodium-helminth co-infection in africa: populations at risk, potential impact on anemia and prospects for combining control. Am J Trop Med Hyg. 2007;77 6 Suppl:88.
11. Namanya DB, Bikaitwoha EM, Berrang-Ford L, Kiconco A, Napyo AK, Namanya DB, et al. Malaria Prevalence and Associated Risk Factors among Batwa Indigenous People of Kanungu District in Southwestern Uganda: Does "Place" Matter? J Biosci Med (Irvine). 2023;11:223–51.
12. Betson M, Sousa-Figueiredo JC, Atuhaire A, Arinaitwe M, Adriko M, Mwesigwa G, et al. Detection of persistent *Plasmodium* spp. infections in Ugandan children after artemether-lumefantrine treatment. Parasitology. 2014;141:1880–90.
13. Keats EC, Kajjura RB, Ataullahjan A, Islam M, Cheng B, Somaskandan A, et al. Malaria reduction drives childhood stunting decline in Uganda: a mixed-methods country case study. Am J Clin Nutr. 2022;115:1559–68.
14. Mulindwa J, Namulondo J, Kitibwa A, Nassuuna J, Nyangiri OA, Kimuda MP, et al. High prevalence of *Schistosoma mansoni* infection and stunting among school age children in communities along the Albert-Nile, Northern Uganda: A cross sectional study. PLoS Negl Trop Dis. 2022;16:e0010570.
15. Kazibwe F, Makanga B, Rubaire-Akiiki C, Ouma J, Kariuki C, Kabatereine NB, et al. Transmission studies of intestinal schistosomiasis in Lake Albert, Uganda and experimental compatibility of local *Biomphalaria* spp. Parasitol Int. 2010;59:49–53.
16. Narcis B. Kabatereine Edridah M. Tukahebwa FK and AWOSB. Epidemiology and geography of *Schistosoma mansoni* in Uganda: implications for planning control. Tropical Medicine and International Health. 2004;9:372–380.
17. Getie S, Wondimeneh Y, Getnet G, Workineh M, Worku L, Kassu A, et al. Prevalence and clinical correlates of *Schistosoma mansoni* co-infection among malaria infected patients, Northwest Ethiopia. BMC Res Notes. 2015;8:480.
18. Orish VN, Ofori-Amoah J, Amegan-Aho KH, Osei-Yeboah J, Lokpo SY, Osisiogu EU, et al. Prevalence of Polyparasitic Infection Among Primary School Children in the Volta Region of Ghana. Open Forum Infect Dis. 2019;6.
19. Zhang Y, Koukounari A, Kabatereine N, Fleming F, Kazibwe F, Tukahebwa E, et al. Parasitological impact of 2-year preventive chemotherapy on schistosomiasis and soil-transmitted helminthiasis in Uganda. BMC Med. 2007;5:1–11.
20. Sokhna C, le Hesran JY, Mbaye PA, Akiana J, Camara P, Diop M, et al. Increase of malaria attacks among children presenting concomitant infection by *Schistosoma mansoni* in Senegal. Malar J. 2004;3:43.

21. Namulondo J, Nyangiri OA, Kimuda MP, Nambala P, Nassuuna J, Egesa M, et al. Transcriptome analysis of peripheral blood of *Schistosoma mansoni* infected children from the Albert Nile region in Uganda reveals genes implicated in fibrosis pathology. PLoS Negl Trop Dis. 2023;17:e0011455.
22. Corstjens PLAM, de Dood CJ, Knopp S, Clements MN, Ortu G, Umulisa I, et al. Circulating Anodic Antigen (CAA): A Highly Sensitive Diagnostic Biomarker to Detect Active *Schistosoma* Infections—Improvement and Use during SCORE. Am J Trop Med Hyg. 2020;103 1 Suppl:50.
23. Corstjens PLAM, De Dood CJ, Kornelis D, Fat EMTK, Wilson RA, Kariuki TM, et al. Tools for diagnosis, monitoring and screening of *Schistosoma* infections utilizing lateral-flow based assays and upconverting phosphor labels. Parasitology. 2014;141:1841–55.
24. Leiden Diagnostic Research Group | LUMC. https://www.lumc.nl/en/afdelingen/parasitologie/leiden-diagnostic-research-group /#!circulating-antigen-detection-for-diagnosis-of-schistosomiasis. Accessed 21 Mar 2024.
25. De Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents .Bull World Health Organisation. 2007;85:660–7.
26. Vinkeles Melchers NVS, van Dam GJ, Shaproski D, Kahama AI, Brienen EAT, Vennervald BJ, et al. Diagnostic Performance of *Schistosom*a Real-Time PCR in Urine Samples from Kenyan Children Infected with *Schistosoma haematobium*: Day-to-day Variation and Follow-up after Praziquantel Treatment. PLoS Negl Trop Dis. 2014;8:e2807.
27. Hoekstra PT, Madinga J, Lutumba P, van Grootveld R, Brienen EAT, Corstjens PLAM, et al. Diagnosis of Schistosomiasis without a Microscope: Evaluating Circulating Antigen (CCA, CAA) and DNA Detection Methods on Banked Samples of a Community-Based Survey from DR Congo. Tropical Medicine and Infectious Disease 2022, Vol 7, Page 315. 2022;7:315.
28. Rantala AM, Taylor SM, Trottman PA, Luntamo M, Mbewe B, Maleta K, et al. Comparison of real-time PCR and microscopy for malaria parasite detection in Malawian pregnant women. Malar J. 2010;9:1–9.
29. Leski TA, Taitt CR, Swaray AG, Bangura U, Reynolds ND, Holtz A, et al. Use of real-time multiplex PCR, malaria rapid diagnostic test and microscopy to investigate the prevalence of *Plasmodium* species among febrile hospital patients in Sierra Leone. Malar J. 2020;19:1–8.
30. Okiring J, Epstein A, Namuganga JF, Kamya E V., Nabende I, Nassali M, et al. Gender difference in the incidence of malaria diagnosed at public health facilities in Uganda. Malar J. 2022;21:1–12.
31. Ayabina DV, Clark J, Bayley H, Lamberton PHL, Toor J, Hollingsworth TD. Gender-related differences in prevalence, intensity and associated risk factors of Schistosoma infections in Africa: A systematic review and meta-analysis. PLoS Negl Trop Dis. 2021;15.
32. Gorreti Zalwango M, Bulage L, Zalwango JF, Migisha R, Agaba BB, Kadobera D, et al. Trends and Distribution of Severe Malaria Cases, Uganda, 2017-2021: Analysis of Health Management Information System Data. Quarterly Epidemiological Bulletin. 2023.
33. McDowell D, Hurt L, Kabatereine NB, Stothard JR, Lello J. Infection History and Current Coinfection With *Schistosoma mansoni* Decreases *Plasmodium* Species Intensities in Preschool Children in

Uganda. J Infect Dis. 2022;225:2181–6.

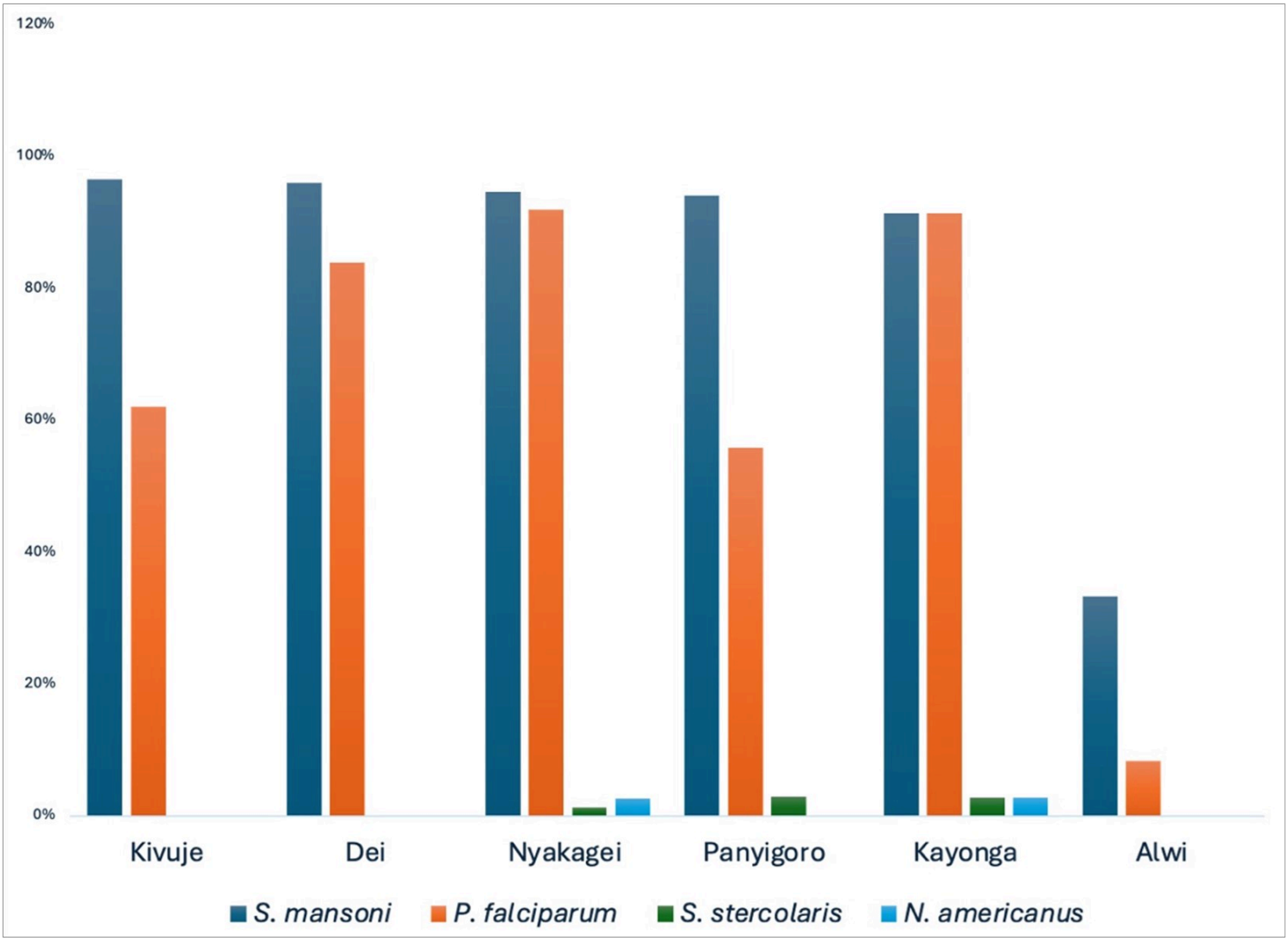
34. Mabbott NA. The Influence of Parasite Infections on Host Immunity to Co-infection With Other Pathogens. Front Immunol. 2018;9:2579.
35. Bucher K, Dietz K, Lackner P, Pasche B, Fendel R, Mordmüller B, et al. *Schistosoma* co-infection protects against brain pathology but does not prevent severe disease and death in a murine model of cerebral malaria. Int J Parasitol. 2011;41:21–31.
36. Kinung'hi SM, Mazigo HD, Dunne DW, Kepha S, Kaatano G, Kishamawe C, et al. Coinfection of intestinal schistosomiasis and malaria and association with haemoglobin levels and nutritional status in school children in Mara region, Northwestern Tanzania: a cross-sectional exploratory study. BMC Res Notes. 2017;10:583.

# Figures



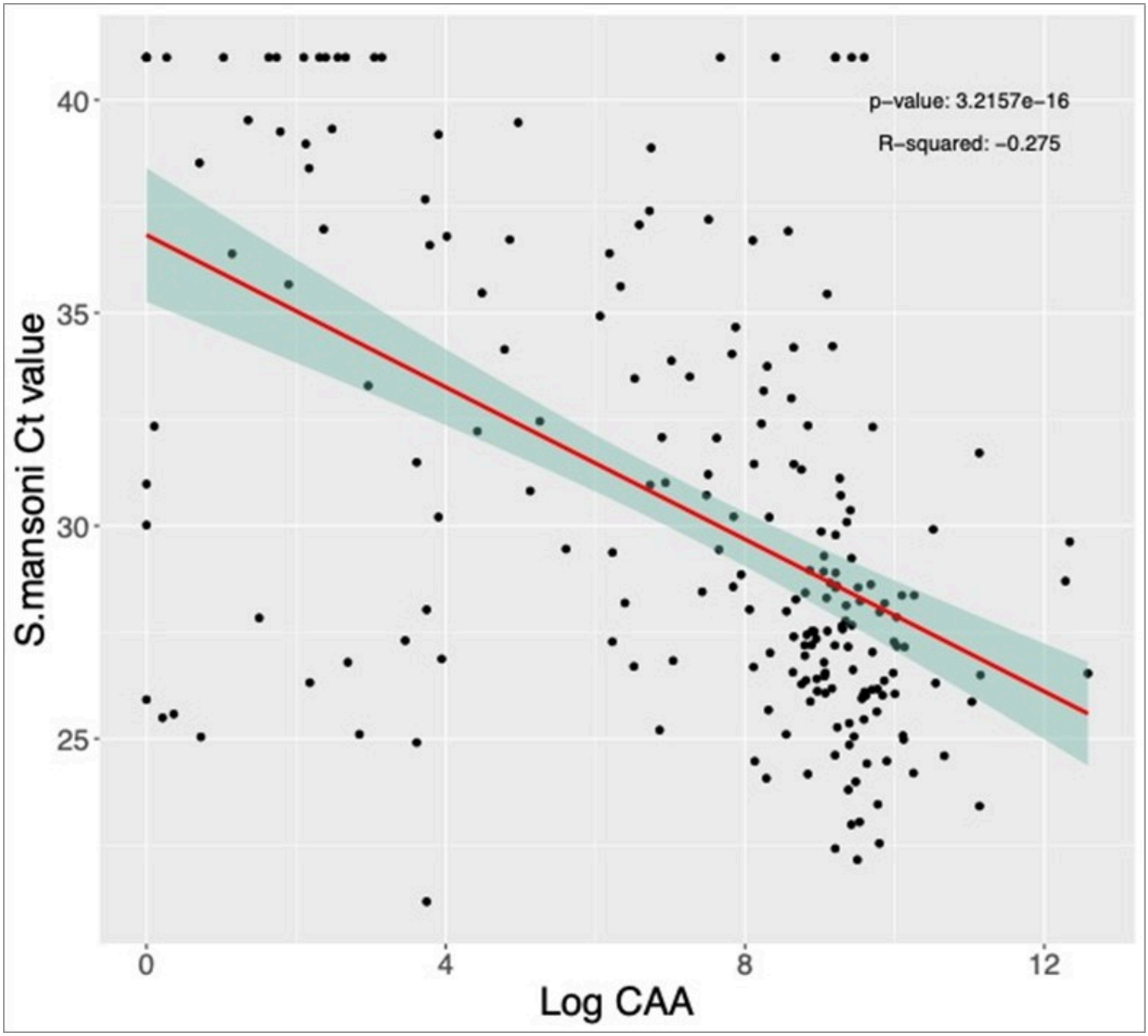

## Figure 1

**A.** Boxplot showing distribution of *P. falciparum* infection among males and females. **B.** Bar graph showing the differences of *P. falciparum* infection between males and females.



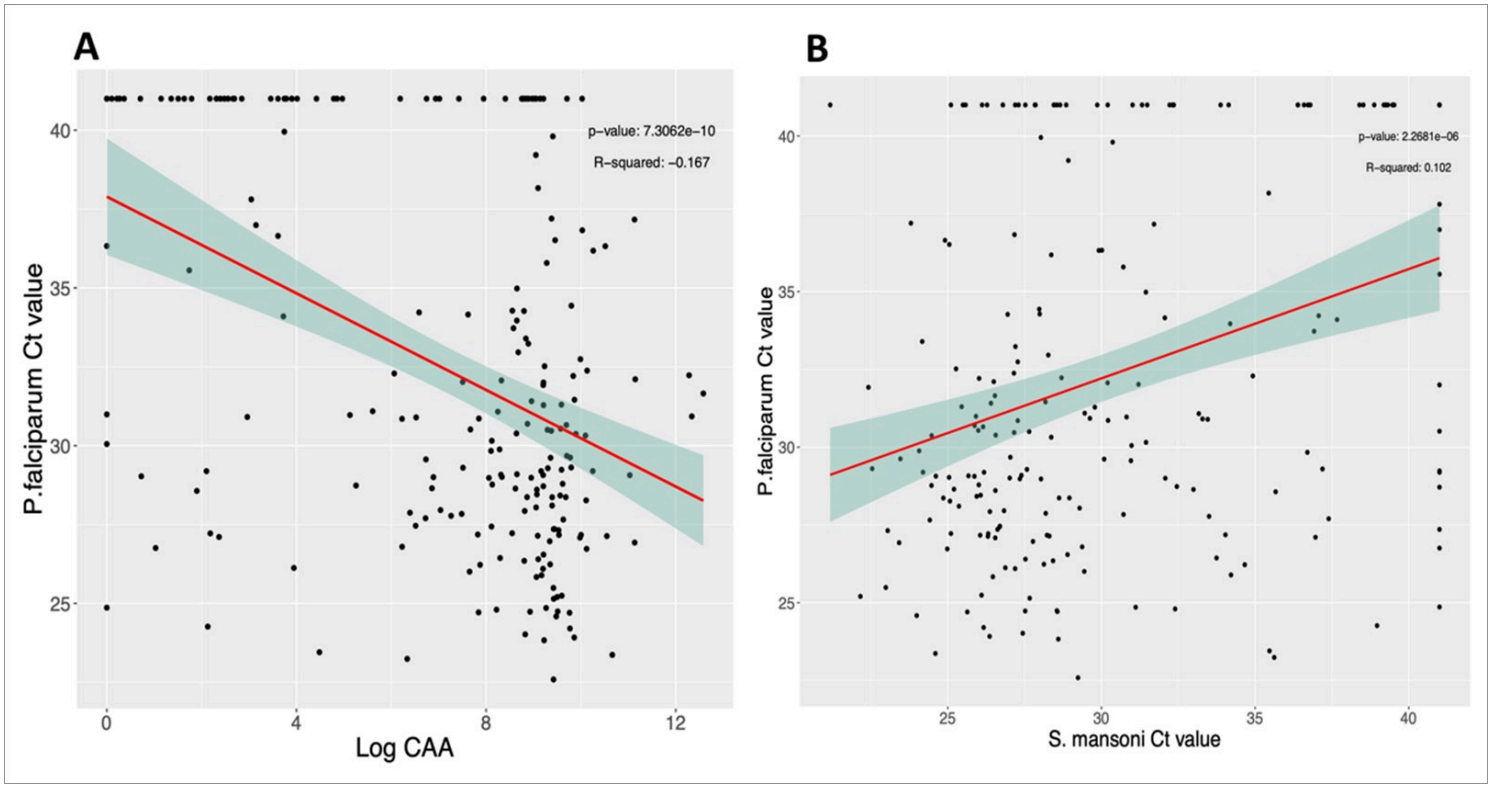

## Figure 2

Graph showing the distribution of the different parasitic infections per site



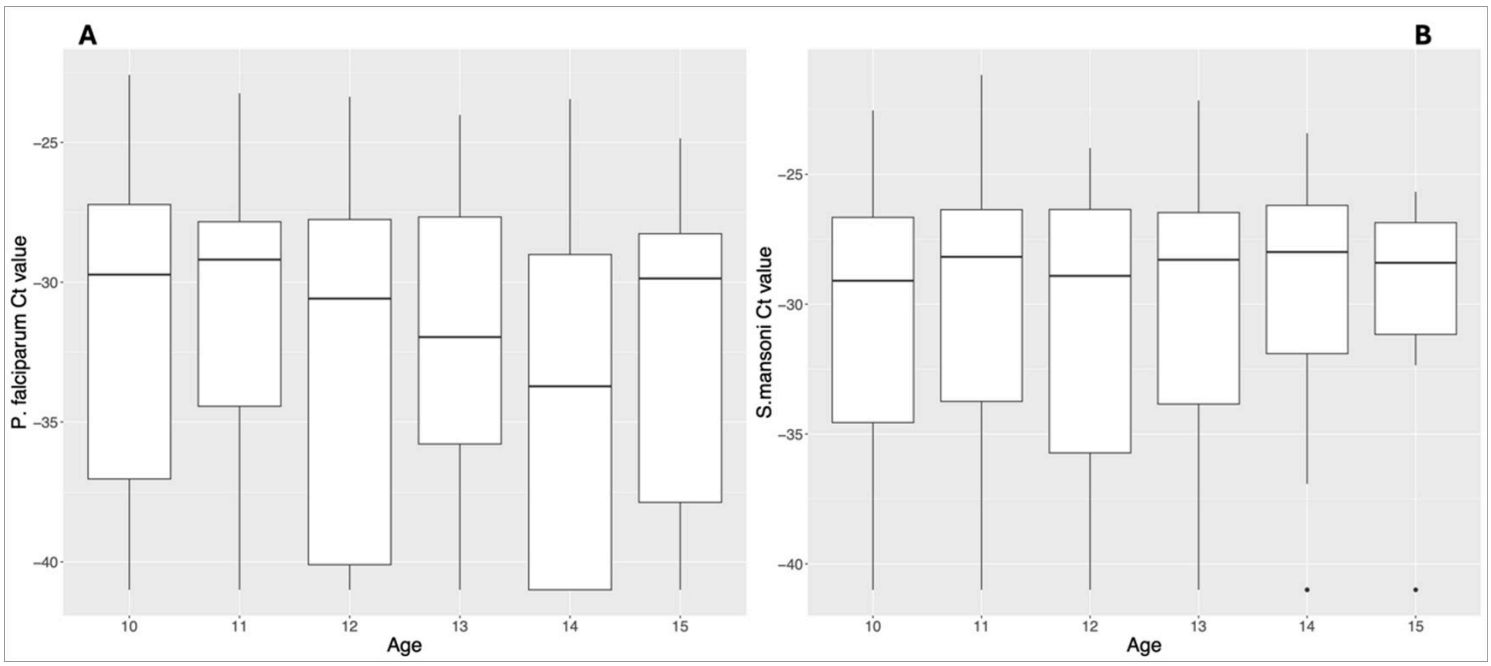

## Figure 3

Correlation between *S.mansoni* PCR test (Ct values) and *S. mansoni* CAA test




## Figure 4

**A.** Correlation between *P. falciparum* infection intensity by PCR and *S. mansoni* infection intensity by CAA. **B.** Correlation between *P. falciparum* infection intensity by PCR and *S. mansoni* infection intensity by PCR




## Figure 5

Box plots of *P.falciparum* infection and *S. mansoni* infection by age

# Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementarydata.docx