RESEARCH ARTICLE

Schistosoma, other helminth infections, and associated risk factors in preschool-aged children in urban Tanzania

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Abstract

Background

Despite the high prevalence of helminth infections among preschool-aged children, control programs in sub-Saharan countries primarily focus on school-aged populations. We assessed the prevalence of helminth infections and determined risk factors for infection among preschool-aged children in the urban setting of Dar es Salaam, Tanzania.

Methodology

Starting in October 2015, we conducted a 12-month prospective study among tuberculosis (TB)-exposed children under the age of 5 years and unexposed controls from neighboring households. At the time of recruitment, we collected medical histories, assessed development and cognitive functions, and performed medical examinations. We performed full blood cell counts and screened for HIV and malaria. Point-of-care circulating cathodic antigen (POC-CCA), urine filtration, Kato-Katz, FLOTAC, and Baermann tests were employed to detect helminth infections in urine and stool. Helminth infections were stratified for Schistosoma and other helminths to identify risk factors, using logistic regression.

Principal findings

We included 310 children with a median age of 26 months (inter quartile range 17–42 months) in the study. Among these, 189 were TB-exposed and 121 TB-unexposed. Two thirds of the children were anemic (hemoglobin level <11 g/dl) and the HIV prevalence was 1.3%. Schistosoma spp. was the predominant helminth species (15.8%; 95% confidence interval [CI] 12.1–20.3%). Other helminth infections were less frequent (9.0%, 95% CI 6.3–12.8%). Poor hygiene, use of household water sources, and TB-exposure were not associated with helminth infection. Development and cognitive scores did not significantly differ in...
helminth-infected and uninfected peers, but hemoglobin levels were significantly lower in helminth-infected children (10.1 g/dl vs. 10.4 g/dl, p = 0.027).

Conclusions/significance
In Dar es Salaam, a city with more than 4 million inhabitants, the prevalence of *Schistosoma* spp. infection among preschool-aged children was unexpectedly high. Setting-specific interventions that target preschool-aged children and urban settlements should be considered to reduce the transmission of *Schistosoma* and other helminth infections and to improve children’s health.

Author summary
In many African countries, children under the age of 5 years are at considerable risk of acquiring parasitic worm infections. Yet, most of the neglected tropical disease control programs in Africa do not include preschool-aged children in deworming campaigns. Chronic parasitic worm infections may impair children’s growth and their cognitive development. We conducted a 12-month prospective study of children younger than 5 years in the Temeke district, Dar es Salaam—the economic capital of Tanzania—to assess the prevalence of parasitic worm infections. Among 310 included children, we found that one in six children was infected with the blood fluke *Schistosoma*, while one in 11 children were infected with soil-transmitted helminths. Anemia was found among 65% of children, particularly among those infected with parasitic worms. The high prevalence of *Schistosoma* infection in this urban setting, despite improved water supply and sanitation as well as limited open freshwater contact shows the pressing need to identify parasitic worm transmission hotspots in urban areas. Setting-specific interventions targeting preschool-aged children and urban settlements, among others, should be considered to reduce the transmission of *Schistosoma* and other parasitic worm infections.

Introduction
Helmint infections affect more than 1.5 billion people globally and are particularly common amongst economically deprived populations [1, 2]. The burden of helminthiases is high in settings with inadequate sanitation, overcrowding, and low socioeconomic status; the same characteristics that govern transmission of tuberculosis (TB) [3–7]. Helminth infections, though rarely fatal, cause considerable morbidity [8, 9]. In children, heavy intensity helmint infections can impair physical growth and cognitive development, and lead to micronutrient deficiencies and anemia [3, 10]. Subsequently, if anemia and its underlying causes are not managed, it may lead to death in children with additional co-morbidities [11, 12]. Children with poor cognitive development have difficulties learning and perform poorly at school, thereby failing to reach their full potential [13]. Chronic helmint infection is also detrimental to the functioning of the immune response against infectious diseases such as TB and, hence, increases the risk of developing TB in later life [14]. Associations between TB and helminth infections have been reported for school-aged and adult populations [6, 15].

Children living in resource-constrained areas in sub-Saharan Africa and elsewhere are at high risk of acquiring helmint infections, given their poor hygienic environments and unattended outdoor access when playing with peers. Early detection and effective management of
Helmint infection can improve children’s health and well-being. Most studies of helminth infections have focused on school-aged populations, though preschool-aged children in highly endemic areas might also show high infection rates [16]. For example, a community-based, cross-sectional survey conducted in Nairobi found that the soil-transmitted helminth prevalence among preschool-aged children was similar to that of school-aged children [17]. In 2008, the World Health Organization (WHO) set an ambitious goal to reach 100% anthelmintic drug coverage by 2012 in endemic countries [18]. Yet, the WHO did not include preschool-aged children in targeted deworming campaigns until 2008.

In 2009, Tanzania adopted the WHO initiative to integrate preventive chemotherapy into its neglected tropical diseases control program, which also covers helminthiases. To date, the focus has been on school-aged children and adults [19]. No universal guidelines exist for using chemotherapy to prevent various helminth infections in preschoolers. To assess the prevalence and intensity of helminth infections among preschool-aged children, including its impact on clinical outcomes, we conducted a cross-sectional survey in an urban setting in Temeke district, Dar es Salaam, Tanzania. We employed a suite of standardized, quality-controlled diagnostic methods to enhance the accuracy of species-specific helminth detection and quantification [20].

Methods

Ethics statement

The study was approved by the Institutional Review Board of the Ifakara Health Institute (reference no. IHI/IRB 12–2015), the Medical Research Coordinating Committee of the National Institute of Medical Research in Tanzania (reference no. NIMR/HQ/R.8a/Vol. IX/2002), and the Ethics Committee of Northwestern and Central Switzerland (reference no. EKNZ UBE-15/49). Children were enrolled after their parents or caregivers gave written informed consent.

Infections with *Schistosoma* spp. were treated with praziquantel (40 mg/kg), soil-transmitted helminths with albendazole (200 or 400 mg depending on children’s age), and *Strongyloides stercoralis* with ivermectin (3 mg), immediately after diagnosis [21]. Additionally, children with a history of TB exposure without active disease were started on isoniazid preventive therapy (20 mg/kg) [22]. Children with anemia (hemoglobin <11 g/dl) were given iron or folic acid supplements, as clinically appropriate. In addition, dietary counseling was provided to parents and caregivers of all children with impaired nutritional status. Human immunodeficiency virus (HIV)-positive children were referred to a care and treatment center for further management, in line with Tanzanian guidelines.

Study setting

The study was carried out in the Temeke district, Dar es Salaam, Tanzania [7] between October 2015 and September 2016. The district has routine TB contact tracing in place supported by TB patients who successfully completed treatment. Mass deworming in the district is coordinated by the neglected tropical disease control coordinator. Although the local water authority supplies piped water to the district, due to the high demand, residents also use ground water sources from boreholes for household chores which is vulnerable to pollution from pit latrines. This borehole water is used by most of the residents in the district [23].

Study design

The current manuscript used the baseline data of a case-control study pertaining to the epidemiology of TB and helminth coinfections among children exposed and not exposed to TB.
Preschool-aged children were recruited from households with an adult TB case (sputum smear-positive for acid-fast bacilli) and from TB-free neighboring households (to serve as controls), based on previously described standard operating procedures [24]. In the present cross-sectional study embedded within the aforementioned case-control study, we assessed the prevalence of helminth infections and determined associations with household characteristics, child development and cognition, and hematological factors in the surveyed children.

Study population and sample size
We aimed for a sample size of 308 children, aged 6–59 months, with 154 TB-exposed and 154 TB-unexposed preschool-aged children, and with one child recruited per household. This sample size would allow estimating local helminth prevalence with a precision of 5% and at an error probability of 5% if the helminth prevalence were of the order of 30%.

Study procedures
Children were seen by trained study clinicians who collected sociodemographic and socioeconomic information and obtained their medical history, including prior illnesses and use of medication. Clinicians assessed children for TB signs and symptoms [22]. A TB-exposure score chart from South Africa was employed to assess TB exposure [25]. The TB score was then categorized into (i) not likely to have TB infection (score of 1–6), or (ii) presumptively TB infected (score of ≥7). In addition, all children had a chest X-ray done. Trained study nurses recorded anthropometric measurements (height and weight), collected samples (blood, urine, stool, adhesive tape slide, and induced sputum), and performed development and cognitive assessments (gross motor, fine motor, language, and social components).

On the day of enrollment, parents or caregivers were given two empty containers labeled with the participant’s unique identification number and invited to submit one fresh morning stool sample and one urine sample of their child the following day. The samples were transferred to a nearby laboratory within 3 hours of collection. Due to limited financial and human resources, only a single stool and urine sample could be collected. Additionally, each participant was provided with a plastic pocket that contained an adhesive tape (50 x 20 mm) and a pre-labeled glass slide and asked to submit the slide with the anal adhesive tape for Enterobius vermicularis examination as described elsewhere [26]. We collected venous blood samples for full blood cell (FBC) counts and for malaria and HIV screening, along with induced sputum samples for microbiological investigation. All samples were received at Temeke clinic, transferred to a laboratory in appropriate temperature-controlled cooler boxes, and processed within 5 hours of receipt.

Cognitive assessment
A validated Malawi Development Assessment Tool (MDAT) that was translated into Kiswahili was used to assess children’s development and cognition [27]. A medical doctor with expert training in pediatrics [28] trained the study nurses before commencing the study. Monthly refresher trainings were conducted on site for the duration of the study. Each child was assessed for 40 min. Parents or caregivers of acutely ill children were advised to return within a week of the child’s recovery for assessment [28].

Laboratory procedures
Helminth investigations. A single stool sample was obtained from each child, subjected to triplicate Kato-Katz thick smears, and examined under a microscope by trained laboratory
technicians for species-specific diagnosis of helminth infection. Triplicate Kato-Katz thick smear slides and the FLOTAC methods were employed for the diagnosis of *Ascaris lumbricoides*, hookworm, *Hymenolepis diminuta*, *Schistosoma mansoni*, and *Trichuris trichiura* while the Baermann technique was used to detect larvae of *Strongyloides stercoralis* [29]. The adhesive tapes were examined under a microscope for *E. vermicularis* eggs [26]. To screen for *S. haematobium* eggs, urine samples underwent urine filtration in duplicates using a hydrophilic polycarbonate membrane filter with a pore size of 20 μm (Sterlitech; Kent, United States of America) and subsequent examination of the filters for *S. haematobium* eggs. Microhemiaturia was examined by reagent strips (Hemastix; Siemens Healthcare Diagnostics, Eschborn, Germany). Urine samples were additionally tested for *Schistosoma* spp. antigens using a point-of-care circulating cathodic antigen (POC-CCA) cassette test (Rapid Medical Diagnostics; Pretoria, South Africa) which has been primarily validated for *S. mansoni*, but cross-reactivity has been reported [20, 30]. Using a visual aid tool and based on a semi-quantitative score, the POC-CCA results were interpreted as negative, trace, 1+, 2+, or 3+. All slides with adhesive tapes, Kato-Katz thick smears, and urine filters were stored in boxes, and 10% of the slides were re-examined for quality control purposes by experienced laboratory technicians within 6 months [29]. All helminth investigations were conducted at the Bagamoyo Research and Training Centre. The standard operating procedures have been described in detail elsewhere [31].

**Microbiological investigations.** Xpert MTB/RIF (Cepheid; Sunnyvale, CA, United States of America) was performed on induced sputum samples at the Temeke district hospital laboratory to aid in the diagnosis of TB. The laboratory is continuously monitored for quality by the Central Tuberculosis Reference Laboratory (Dar es Salaam, Tanzania).

**Blood testing.** Blood samples were screened for malaria with a rapid diagnostic test (Access Bio; Somerset, NJ, United States of America), and for HIV infection using Alere Determine HIV-1/2 (Alere; Waltham, MA, United States of America) if the child’s age was ≥18 months or RNA polymerase chain reaction if <18 months. The FBC were done with an MS4 Vet hematology analyzer (Diamond Diagnostics; Massachusetts, United States of America) to determine hematological indices such as hemoglobin, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and red blood cell distribution width (RCDW).

**Data collection and definitions**

Data were recorded into tablet computers, using open data kit (ODK; [http://opendatakit.org/](http://opendatakit.org/)) and “odk Planner”, a data management tool. Laboratory results were entered into ODK from paper forms.

A helminth infection was defined as positive when eggs or larvae of the following species were microscopically identified: *A. lumbricoides, E. vermicularis*, hookworm, *H. diminuta, S. haematobium, S. mansoni, S. stercoralis*, or *T. trichiura*. Subsequently, helminth infections were grouped into (i) schistosomiasis, defined as infection with either *S. mansoni* or *S. haematobium* (based on stool microscopy, using Kato-Katz thick smears, urine filtration and/or positive POC-CCA urine cassette test results) and (ii) other helminthiasis, including infections with any of the other helminths (*A. lumbricoides, H. diminuta*, hookworm, *T. trichiura, E. vermicularis, and S. stercoralis*). A POC-CCA test was regarded as positive if the band revealed 1+, 2+, or 3+. In sensitivity analyses, POC-CCA definition included also trace-positive results.

In the absence of any signs or symptoms suggestive of TB and/or as ascertained by Xpert MTB/RIF, a child was considered presumptively TB infected if the TB exposure score was ≥7 and unlikely to have a TB infection if the score was 1–6 [25]. Anemia was defined as hemoglobin <11.0 g/dl, as per WHO recommendations [32]. Anthropometric z-scores were calculated.
using the 2006 WHO Growth Standards in Stata version 13.1 (Stata Corporation; College Station, TX, United States of America) using the ‘zscore06’ command [33].

Statistical analysis
Absolute frequencies and proportions were used to describe children, parents/caretakers, and household characteristics overall and stratified by the two groups of helminthiases. A measure of socioeconomic status was derived from a factor analysis of household asset variables and defined as low or high for score values below and above the median, respectively. Clinical outcomes included anemia, cognitive score and anthropometric measures (weight and height). We performed mixed logistic regression analyses with random intercepts at the level of matched pairs to identify risk factors for helminth infection, considering schistosomiasis and other helminthiases. We constructed multivariable core models comprising age, sex, type of toilet, hygiene behavior, and parent education variables based on clinical relevance and added other variables as appropriate, one by one. We also performed a sensitivity analysis to identify risk factors for Schistosoma spp. infection using the core model as above and considering trace results in the POC-CCA urine cassette test as positive. We used box-plots to compare the four MDAT components in children with and without helminth infections and calculated the overall median and interquartile range (IQR) of the total MDAT score and across relevant subsamples. We dichotomized the four components of the MDAT score at their median and ran mixed logistic regressions to compare scores between helminth-infected and uninfected children. We also compared hematological indices according to the presence of helminth infections using mixed linear regression models. All analyses were performed in Stata version 13.1 (Stata Corporation; College Station, United States of America).

Results
Study flow and baseline characteristics of children
We invited 398 parents and caregivers with children aged 6–59 months to participate. Parents/caregivers of 325 children consented and their children were enrolled. Of those, 310 completed the study procedures. Eight children did not provide their sociodemographic and clinical information, six did not submit stool and urine samples for helminth diagnosis, and one parent withdrew consent (Fig 1).

Of the 310 participating children, 160 (52%) were girls and the median age was 26 months (IQR: 17–42 months, range 6–58 months). The median height-for-age Z-score (HAZ) was -1.14 (95% confidence interval (CI): -1.91 to -0.20) (Table 1). A total of 189 (61%) children were exposed to smear-positive adult pulmonary TB patients and four (1.3%) were HIV-positive. Twenty-nine (9.4%) mothers reportedly tested HIV-positive during pregnancy. Fourteen (4.5%) children had a positive malaria rapid diagnostic test, six (1.9%) reportedly received anthelmintics within 3 months prior to enrollment in the study. Parents/caretakers of 23 (7.4%) children reported having moved from other regions to Dar es Salaam after their children were born.

Prevalence of helminth infections
The overall prevalence of Schistosoma spp. infection was 15.8% (95% CI 12.1–20.3%). Schistosoma spp. infection as determined by POC-CCA, was found in 47 children (15.2%; 95% CI 11.6–19.6%), S. haematobium eggs were only found in the urine of three individuals (1.0%) (Table 2), and no S. mansoni eggs were found in any of the Kato-Katz thick smears or FLOTAC examinations. There was no difference in the distribution of children with Schistosoma
spp. infection in young (6–24 months) and older (25–59 months) age groups (53% vs. 47%, p = 0.3) or between boys and girls (51% vs. 49%, p = 0.7). There was also no significant difference between TB-exposed and unexposed children (67% vs. 60%, p = 0.3), as shown in Table 1. The prevalence of Schistosoma spp. infection (as determined by POC-CCA) increased to 31.0% (95% CI 26.3–36.7%) when considering trace results as positive.

The prevalence of other helminth species infections, excluding Schistosoma spp., was 9.0% (95% CI 6.3–12.8%). The most frequently detected helminth species was S. stercoralis (16 children; 5.2%), followed by E. vermicularis (6; 1.9%), and hookworm (6; 1.9%). Infections with A. lumbricoides and H. diminuta were found in only one child each, and no T. trichiura infection was observed (Table 2). The difference in the distribution of helminth infections between TB-exposed and unexposed children was not statistically significant (62% vs. 54%, p = 0.4).

Five children (1.6%) had dual species helminth infections: two with Schistosoma spp.-S. stercoralis; and one each with Schistosoma spp.-E. vermicularis, E. vermicularis-hookworm, and A. lumbricoides-H. diminuta. One child had a triple species helminth infection with Schistosoma spp.-E. vermicularis-hookworm.
Table 1. Baseline sociodemographic, socioeconomic, and clinical characteristics of 310 preschool-aged children in a study conducted between October 2015 and September 2016, and their parents/caregivers in the Temeke district, Dar es Salaam, Tanzania.

| Characteristic | All (n = 310) | Any helminth species 1 | Schistosoma spp. 2 |
|---------------|--------------|------------------------|-------------------|
|               | Infected (n = 74) | Not infected (n = 236) | Infected (n = 49) | Not infected (n = 261) |
| Child characteristics | | | |
| Age (months), median (IQR) | 26 (17–42) | 23 (17–36) | 28 (17–43) | 23 (18–38) | 27 (16–42) |
| Age groups (months) | | | | | |
| 6–12 | 52 (17) | 11 (15) | 41 (17) | 8 (16) | 44 (17) |
| 13–24 | 92 (30) | 29 (39) | 63 (27) | 18 (36) | 74 (28) |
| 25–36 | 71 (23) | 16 (22) | 55 (23) | 10 (21) | 61 (24) |
| 37–48 | 57 (18) | 10 (14) | 47 (20) | 7 (14) | 50 (19) |
| 49–59 | 38 (12) | 8 (11) | 30 (13) | 6 (13) | 32 (12) |
| Sex | | | | | |
| Female | 160 (52) | 37 (50) | 123 (52) | 24 (49) | 136 (52) |
| Male | 150 (48) | 37 (50) | 113 (48) | 25 (51) | 125 (48) |
| Delivered by | | | | | |
| Caesareaan section | 40 (13) | 13 (17) | 27 (11) | 10 (20) | 30 (12) |
| SVD | 253 (20) | 56 (76) | 197 (84) | 38 (76) | 215 (82) |
| Unknown | 17 (5) | 5 (7) | 12 (5) | 1 (2) | 16 (6) |
| Born at gestation age (weeks) | | | | | |
| Pre-term <37 | 9 (3) | 2 (2) | 7 (3) | 1 (2) | 8 (3) |
| Term ≥37 | 284 (92) | 67 (91) | 217 (90) | 45 (96) | 239 (91) |
| Unknown | 17 (5) | 5 (7) | 12 (5) | 1 (2) | 16 (6) |
| Birth weight (kg) | | | | | |
| Low <2.5 | 28 (9) | 5 (7) | 24 (10) | 4 (8) | 25 (10) |
| Normal ≥2.5 | 265 (86) | 64 (86) | 200 (85) | 44 (09) | 220 (84) |
| Unknown | 17 (5) | 5 (7) | 12 (5) | 1 (2) | 16 (6) |
| Immunization status | | | | | |
| BCG, with scar | 306 (99) | 260 (85) | 71 (96) | 235 (99) | 42 (86) | 218 (84) |
| Measles | 263 (85) | 68 (92) | 195 (83) | 46 (94) | 217 (83) |
| HIV status | | | | | |
| Positive | 4 (1.3) | 2 (3) | 2 (1) | 0 | 4 (2%) |
| Negative | 306 (98.7) | 72 (97) | 234 (99) | 49 (100) | 257 (98) |
| Hemoglobin level (g/dl) | | | | | |
| Anemic <11.0 | 203 (65) | 56 (76) | 147 (62) | 35 (71) | 168 (64) |
| Not anemic ≥11.0 | 104 (34) | 17 (23) | 87 (37) | 13 (27) | 91 (35) |
| Missing | 3 (1) | 1 (1) | 2 (1) | 1 (2) | 2 (1) |
| Malaria rapid diagnostic test | | | | | |
| Positive | 14 (5) | 3 (4) | 11 (5) | 3 (6) | 11 (4) |
| Negative | 296 (95) | 71 (96) | 225 (95) | 46 (94) | 250 (96) |
| TB exposure history | | | | | |
| Exposed | 189 (61) | 46 (62) | 143 (61) | 33 (67) | 156 (60) |
| Unexposed | 121 (39) | 28 (38) | 93 (39) | 16 (33) | 105 (40) |
| TB exposure score | | | | | |
| Likely not infected | 197 (64) | 50 (68) | 147 (62) | 33 (67) | 164 (63) |
| Likely infected | 113 (36) | 24 (32) | 89 (38) | 16 (33) | 97 (37) |
| Deworming status (past 3 months) | | | | | |
| Not dewormed | 304 (98) | 72 (97) | 232 (98) | 48 (98) | 256 (98) |
| Dewormed | 6 (2) | 2 (3) | 4 (2) | 1 (2) | 5 (2) |

(Continued)
Table 1. (Continued)

| Characteristic                  | All (n = 310) | Any helminth species ¹ (n = 74) | Schistosoma spp. ² (n = 97) |
|---------------------------------|--------------|----------------------------------|-------------------------------|
| n (%)                           | Infected     | Not infected                     | Infected                     | Not infected               |
|                                 | (n = 74)     | (n = 236)                        | (n = 49)                     | (n = 261)                  |
| **HAZ-scores**                  |              |                                  |                              |                             |
| Median (IQR)                    | -1.14 (-1.91 to -0.2) | -1.16 (-1.72 to -0.07) | -1.12 (-1.94 to -0.33) | -1.17 (-1.58 to -0.13) |
| **WAZ-score**                   |              |                                  |                              |                             |
| Median (IQR)                    | -1.14 (-2.07 to -0.35) | -1.3 (-2.22 to -0.28) | -1.12 (-1.99 to -0.35) | -1.34 (-2.36 to -0.69) |
| **WHZ-score**                   |              |                                  |                              |                             |
| Median (IQR)                    | -0.94 (-2.02 to -0.13) | -1.16 (-2.02 to -0.17) | -0.79 (-1.86 to -0.13) | -1.48 (-2.07 to -0.10) |

**Household characteristics**

**Number of people**

|       | All     | Infected (n = 74) | Not infected (n = 236) | Schistosoma spp. ² (n = 97) |
|-------|---------|-------------------|------------------------|-----------------------------|
| <6    | 190 (61)| 43 (58)           | 147 (62)               | 29 (59)                     |
| ≥6    | 120 (39)| 31 (42)           | 89 (38)                | 20 (41)                     |

**Household income per month (US$)**

|       | All     | Infected (n = 74) | Not infected (n = 236) | Schistosoma spp. ² (n = 97) |
|-------|---------|-------------------|------------------------|-----------------------------|
| <100  | 108 (35)| 28 (38)           | 80 (34)                | 15 (31)                     |
| ≥100  | 202 (65)| 46 (62)           | 156 (66)               | 34 (69)                     |

**Water source for household chores**

|       | All     | Infected (n = 74) | Not infected (n = 236) | Schistosoma spp. ² (n = 97) |
|-------|---------|-------------------|------------------------|-----------------------------|
| Bore well | 90 (29) | 15 (20)           | 27 (11)                | 14 (29)                     |
| Tap    | 153 (49)| 43 (58)           | 158 (67)               | 27 (55)                     |
| Unknown | 67 (22) | 16 (22)           | 51 (22)                | 8 (16)                      |

**Type of household toilet**

|       | All     | Infected (n = 74) | Not infected (n = 236) | Schistosoma spp. ² (n = 97) |
|-------|---------|-------------------|------------------------|-----------------------------|
| Septic tank | 93 (30) | 28 (38)           | 65 (28)                | 21 (43)                     |
| Pit latrine | 217 (70)| 46 (62)           | 171 (72)               | 28 (57)                     |

**Hygienic practices**

|       | All     | Infected (n = 74) | Not infected (n = 236) | Schistosoma spp. ² (n = 97) |
|-------|---------|-------------------|------------------------|-----------------------------|
| Poor  | 36 (12) | 12 (16)           | 24 (10)                | 7 (14)                      |
| Good  | 274 (88)| 62 (84)           | 212 (90)               | 42 (86)                     |

**SES**

|       | All     | Infected (n = 74) | Not infected (n = 236) | Schistosoma spp. ² (n = 97) |
|-------|---------|-------------------|------------------------|-----------------------------|
| Low   | 159 (50)| 40 (54)           | 119 (50)               | 28 (57)                     |
| High  | 151 (50)| 34 (46)           | 127 (50)               | 21 (43)                     |

**Parent/caregiver characteristics**

**Mothers prior pregnancies**

|       | All     | Infected (n = 74) | Not infected (n = 236) | Schistosoma spp. ² (n = 97) |
|-------|---------|-------------------|------------------------|-----------------------------|
| Unknown | 17 (5) | 5 (7)             | 12 (5)                 | 1 (2)                       |
| 0     | 88 (30)| 19 (26)           | 69 (29)                | 9 (19)                      |
| 1–2   | 142 (48)| 39 (53)           | 103 (44)               | 30 (64)                     |
| ≥3    | 63 (17)| 11 (15)           | 52 (22)                | 7 (15)                      |

**Mothers HIV status during pregnancy**

|       | All     | Infected (n = 74) | Not infected (n = 236) | Schistosoma spp. ² (n = 97) |
|-------|---------|-------------------|------------------------|-----------------------------|
| Unknown | 24 (8) | 6 (8)             | 18 (7)                 | 1 (2)                       |
| Positive | 29 (9)| 4 (5)             | 25 (11)                | 3 (6)                       |
| Negative | 257 (83)| 64 (86)         | 193 (82)               | 45 (92)                     |

**Mothers marital status**

|       | All     | Infected (n = 74) | Not infected (n = 236) | Schistosoma spp. ² (n = 97) |
|-------|---------|-------------------|------------------------|-----------------------------|
| Single | 76 (25)| 19 (25)           | 57 (24)                | 14 (29)                     |
| Married | 217 (70)| 50 (68)          | 167 (71)               | 34 (69)                     |
| Unknown | 17 (5) | 5 (7)             | 12 (5)                 | 1 (2)                       |

**Parent education level**

|       | All     | Infected (n = 74) | Not infected (n = 236) | Schistosoma spp. ² (n = 97) |
|-------|---------|-------------------|------------------------|-----------------------------|
| No or primary education | 244 (79)| 63 (85)           | 181 (77)               | 42 (86)                     |
| Secondary/higher education | 66 (21)| 11 (15)           | 55 (23)                | 7 (14)                      |

(Continued)
Schistosoma spp. infection was significantly associated with having a septic tank toilet in the household (adjusted odds ratio (aOR) 2.04, 95% CI: 1.02–4.07, p = 0.042; Table 3). Higher education of parents/caregivers, tap water at home, and better hygiene practices showed no significant association with Schistosoma spp. infection. Additionally, Schistosoma spp. infection was similar in TB-exposed and unexposed children (aOR 1.34, 95% CI: 0.67–2.68, p = 0.4) (Table 3). In the sensitivity analysis that considered POC-CCA trace results as positive, none of the variables included in the core model, including having septic tank toilets, were associated with Schistosoma spp. infection (Table S1). Furthermore, none of the risk factors were significantly associated with any of the other helminth infection, including having a septic tank toilet (aOR 0.92, 95% CI: 0.35–2.40, p = 0.9) (Table 3).

The overall median MDAT score in the study population was 3.30 (IQR 2.78–3.49). There was no significant difference in the overall median cognitive score in helminth-infected and uninfected children (3.20 [95% CI 2.74–3.44] vs. 3.33 [95% CI 2.80–3.50], p = 0.2 (Table S2). There was also no effect of Schistosoma spp. infection on the overall median cognitive score among the two groups (3.17 [95% CI 2.78–3.44] vs. 3.32 [95% CI 2.78–3.50], p = 0.2).

The median gross motor score tended to be higher among preschool-aged children with a helminth infection compared to their uninfected peers. The median fine motor (0.79 vs. 0.83), social (0.85 vs. 0.89), and language scores (0.86 vs. 0.88) tended to be lower among helminth-infected compared to helminth-uninfected children (Fig 2), but none of the differences achieved statistical significance.

### Table 1. (Continued)

| Characteristic                        | All (n = 310) | Any helminth species | Schistosoma spp. |
|---------------------------------------|--------------|----------------------|------------------|
|                                       | Infected (n = 74) | Not infected (n = 236) | Infected (n = 49) | Not infected (n = 261) |
| Parent occupation                     |              |                      |                  |
| Unemployed                            | 196 (63)    | 49 (66)              | 147 (62)         | 31 (63)              |
| Employed                              | 114 (37)    | 25 (34)              | 89 (38)          | 18 (37)              |
| Family migration history since child birth |          |                      |                  |
| Migrated                              | 23 (7)      | 8 (11)               | 15 (6)           | 3 (6)                |
| Did not migrate                       | 189 (61)    | 44 (59)              | 144 (61)         | 36 (73)              |
| Unknown                               | 98 (32)     | 22 (30)              | 77 (33)          | 10 (20)              |

HAZ, height for age, moderate to severe stunting (z-score ≤ -2); HIV, human immunodeficiency virus; TB exposure score based on Mandalakas et al. [25]; SVD, spontaneous vaginal delivery; WAZ, weight for age, moderate to severe underweight (z-score ≤ -2); WHZ, weight for height, moderate to severe wasting (z-score ≤ -2); US$, United States dollars (1 US$ = 2,190 Tanzanian Shillings); SES, socioeconomic status (low = below median of the principal asset score, high = above the median of the principal asset score)

1 Any helminth infection defined as positive when eggs or larvae of the following species were microscopically identified: A. lumbricoides, E. vermicularis, hookworm, H. diminuta, S. haematobium, S. mansoni, S. stercoralis, or T. trichiura; or a positive POC-CCA urine cassette test result indicating Schistosoma spp. infection (test result 1+, 2+, or 3+)

2 Schistosoma spp. includes S. mansoni and S. haematobium

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### Risk factors for helminth infections

Schistosoma spp. infection was significantly associated with having a septic tank toilet in the household (adjusted odds ratio (aOR) 2.04, 95% CI: 1.02–4.07, p = 0.042; Table 3). Higher education of parents/caregivers, tap water at home, and better hygiene practices showed no significant association with Schistosoma spp. infection. Additionally, Schistosoma spp. infection was similar in TB-exposed and unexposed children (aOR 1.34, 95% CI: 0.67–2.68, p = 0.4) (Table 3). In the sensitivity analysis that considered POC-CCA trace results as positive, none of the variables included in the core model, including having septic tank toilets, were associated with Schistosoma spp. infection (Table S1). Furthermore, none of the risk factors were significantly associated with any of the other helminth infection, including having a septic tank toilet (aOR 0.92, 95% CI: 0.35–2.40, p = 0.9) (Table 3).

### Association of helminth infections with development and cognitive scores

The overall median MDAT score in the study population was 3.30 (IQR 2.78–3.49). There was no significant difference in the overall median cognitive score in helminth-infected and uninfected children (3.20 [95% CI 2.74–3.44] vs. 3.33 [95% CI 2.80–3.50], p = 0.2 (Table S2). There was also no effect of Schistosoma spp. infection on the overall median cognitive score among the two groups (3.17 [95% CI 2.78–3.44] vs. 3.32 [95% CI 2.78–3.50], p = 0.2).

The median gross motor score tended to be higher among preschool-aged children with a helminth infection compared to their uninfected peers. The median fine motor (0.79 vs. 0.83), social (0.85 vs. 0.89), and language scores (0.86 vs. 0.88) tended to be lower among helminth-infected compared to helminth-uninfected children (Fig 2), but none of the differences achieved statistical significance.
Association of helminth infection with hematological parameters

Almost two-thirds of the children (203; 65%) were anemic; nine (4.4%) of those with anemia had a positive rapid malaria diagnostic test result. Moderate anemia (hemoglobin level 7.0–9.9 g/dl) was most prevalent (49%), while mild anemia (hemoglobin 10.0–10.9 g/dl) was found in 44%, and severe anemia (hemoglobin < 7 g/dl) was found in 14 of the anemic children (6.9%).

Five (6%) children with mild anemia, three (3%) with moderate anemia, and one (7%) with severe anemia had malaria.

Anemia was diagnosed in 56 (77%) participants with helminth infections, including all six with hookworm, all three with S. haematobium, the one with A. lumbricoides, and the one with H. diminuta. With regard to Schistosoma spp. infection (as determined by POC-CCA), 33 out of 46 infected had anemia (72%) and 12 of the 16 S. stercoralis-infected children were anemic (75%). Two children with anemia had both helminth infections and malaria.

When comparing hemoglobin and hematological parameters with helminth infection, the median hemoglobin value was significantly lower in helminth-infected children compared with their uninfected peers (10.1 g/dl [IQR 9.1–10.8 g/dl] vs. 10.4 g/dl [IQR 9.4–11.4 g/dl], p = 0.027) (Fig 3). This difference remained significant even when excluding malaria cases (10.4 g/dl [IQR 9.6–11.4 g/dl] vs. 10.1 g/dl [IQR 9.0–10.8], p = 0.014). All other hematological parameters

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**Table 2. Frequency distribution of helminth species among preschool-aged children in Dar es Salaam, Tanzania in a study conducted between October 2015 and September 2016.**

| Helminth infection | All <24 months | >24 months |
|--------------------|---------------|------------|
|                    | Male (% | Female (%) | Male (%) | Female (%) |
| Total              | 310 (100) | 72 (100) | 72 (100) | 78 (100) | 88 (100) |
| Any helminth infection | 74 (23.9) | 25 (34.7) | 15 (20.8) | 12 (15.4) | 22 (25.0) |

**Schistosomiasis**

| Schistosoma spp. (POC-CCA) | Any positive result (trace and positive) | Trace | Positive | 1+ | 2+ | 3+ |
|-----------------------------|-----------------------------------------|-------|----------|----|----|----|
|                             | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Any positive result (trace and positive) | 97 (31.3) | 27 (37.5) | 21 (29.2) | 20 (25.6) | 29 (33.0) |
| Trace | 50 (16.1) | 11 (15.3) | 12 (16.7) | 11 (14.1) | 16 (18.2) |
| Positive | 47 (15.2) | 16 (22.2) | 9 (12.5) | 9 (11.5) | 13 (14.3) |
| 1+ | 34 (11.0) | 8 (11.1) | 9 (12.5) | 6 (7.7) | 11 (12.5) |
| 2+ | 12 (3.9) | 8 (11.1) | 0 (0.0) | 2 (2.6) | 2 (2.3) |
| 3+ | 1 (0.3) | 0 (0.0) | 0 (0.0) | 1 (1.3) | 0 (0.0) |

**Schistosoma haematobium**

| Schistosoma haematobium | Positive | Trace | Positive | 1+ | 2+ |
|-------------------------|----------|-------|----------|----|----|
|                         | n (%) | n (%) | n (%) | n (%) | n (%) |
| Positive | 3 (0.97) | 1 (1.5) | 1 (1.5) | 0 (0.0) | 1 (1.1) |

**Other helminth infection**

| Other helminth infection | Any of the other helminth species | Strongyloides stercoralis | Enterothubus vermicularis | Hookworm | Ascaris lumbricoides | Hymenolepis diminuta |
|--------------------------|----------------------------------|--------------------------|--------------------------|----------|---------------------|---------------------|
|                          | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Any of the other helminth species | 28 (9.0) | 10 (13.9) | 5 (6.9) | 4 (5.1) | 9 (10.2) |
| Strongyloides stercoralis | 16 (5.2) | 6 (8.3) | 3 (4.2) | 3 (3.9) | 4 (4.6) |
| Enterothubus vermicularis | 6 (1.9) | 1 (1.4) | 1 (1.4) | 1 (1.3) | 3 (3.4) |
| Hookworm | 6 (1.9) | 3 (4.2) | 2 (2.8) | 0 (0.0) | 1 (1.1) |
| Ascaris lumbricoides | 1 (0.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (1.1) |
| Hymenolepis diminuta | 1 (0.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (1.1) |

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1 Any helminth was defined as positive when eggs or larvae of the following species were microscopically identified: A. lumbricoides, E. vermicularis, hookworm, H. diminuta, S. haematobium, S. mansoni, S. stercoralis, and T. trichiura
2 Point-of-care circulating cathodic antigen urine cassette test for detection of Schistosoma spp. infection (POC-CCA test result 1+, 2+, or 3+).
3 Based on urine filtration (egg-positive urine filtration)
4 Other helminth species (based on stool or adhesive tape microscopy): A. lumbricoides, E. vermicularis, hookworm, H. diminuta, and S. stercoralis

Five participants had dual species and one participant a triple species helminth infection

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Table 3. Risk factors for *Schistosoma* and soil-transmitted helminth infections among preschool-aged children in Dar es Salaam, Tanzania in a study conducted between October 2015 and September 2016.

| Characteristics                  | All          | Schistosoma spp. | Other helminths |          |          |          |          |          |
|----------------------------------|--------------|------------------|-----------------|----------|----------|----------|----------|----------|
|                                  | All (% n)    | Crude OR (95% CI)p value | Adjusted aOR (95% CI)p value | Crude OR (95% CI)p value | Adjusted aOR (95% CI)p value |
|                                  |              |                  |                  |          |          |          |          |          |
| Age groups (months)              |              |                  |                  |          |          |          |          |          |
| 6–12                             | 52 (17)      | 1.00             | 1.00             | 1.00     | 1.00     |
| 13–24                            | 92 (30)      | 1.33 (0.21–3.40) | 1.31 (0.51–3.40) | 2.36 (0.56–9.86) | 2.38 (0.58–9.78) |
| 25–36                            | 71 (23)      | 0.89 (0.31–2.51) | 0.86 (0.30–2.44) | 0.86 (0.13–4.78) | 0.78 (0.13–4.59) |
| 37–48                            | 57 (18)      | 0.76 (0.25–2.34) | 0.76 (0.24–2.37) | 0.80 (0.27–3.11) | 0.80 (0.11–5.72) |
| 49–59                            | 38 (12)      | 0.76 (0.31–3.32) | 0.92 (0.27–3.11) | 0.80 (0.11–5.83) | 0.80 (0.11–5.72) |
| Sex                              |              |                  |                  |          |          |          |          |          |
| Female                           | 160 (52)     | 1.00             | 1.00             | 1.00     | 1.00     |
| Male                             | 150 (48)     | 1.12 (0.59–2.11) | 1.06 (0.55–2.02) | 1.16 (0.47–2.85) | 1.05 (0.44–2.51) |
| Individual deworming history1    |              |                  |                  |          |          |          |          |          |
| Not dewormed                     | 304 (98)     | 1.00             | 1.00             | 1.00     | 1.00     |
| Dewormed                         | 6 (2)        | 1.07 (0.11–10.12)| 1.06 (0.11–10.1) | 2.14 (0.17–26.84) | 2.24 (0.18–27.20) |
| TB exposure                      |              |                  |                  |          |          |          |          |          |
| Unexposed                        | 121 (39)     | 1.00             | 1.00             | 1.00     | 1.00     |
| Exposed                          | 189 (61)     | 1.43 (0.73–2.82) | 1.34 (0.67–2.68) | 0.72 (0.31–1.67) | 0.74 (0.31–1.74) |
| Number of people in the household|              |                  |                  |          |          |          |          |          |
| <6                               | 190 (61)     | 1.00             | 1.00             | 1.00     | 1.00     |
| ≥6                               | 120 (39)     | 1.13 (0.59–2.16) | 1.13 (0.58–2.20) | 1.47 (0.61–3.53) | 1.49 (0.62–3.54) |
| Water source for household chores|              |                  |                  |          |          |          |          |          |
| Bore well                        | 90 (29)      | 1.00             | 1.00             | 1.00     | 1.00     |
| Tap                              | 153 (49)     | 0.43 (0.21–0.88) | 0.43 (0.20–0.94) | 4.02 (1.04–15.5) | 4.12 (1.05–16.3) |
| Unknown                          | 67 (22)      | 0.41 (0.16–1.02) | 0.41 (0.16–1.08) | 4.22 (0.96–18.5) | 4.90 (1.07–22.3) |
| Type of toilet                   |              |                  |                  |          |          |          |          |          |
| Pit latrine                      | 217 (70)     | 1.00             | 1.00             | 1.00     | 1.00     |
| Septic tank                      | 93 (30)      | 2.03 (1.03–4.00) | 2.04 (1.02–4.07) | 0.98 (0.37–2.57) | 0.92 (0.35–2.40) |
| Hygienic practices2              |              |                  |                  |          |          |          |          |          |
| Poor                             | 36 (12)      | 1.00             | 1.00             | 1.00     | 1.00     |
| Better                           | 274 (88)     | 0.74 (0.29–1.87) | 0.87 (0.34–2.25) | 0.55 (0.17–1.82) | 0.54 (0.16–1.78) |
| Household income per month (US$)3|              |                  |                  |          |          |          |          |          |
| <100                             | 108 (35)     | 1.00             | 1.00             | 1.00     | 1.00     |

(Continued)
Table 3. (Continued)

| Characteristics | All n (%) | Schistosoma spp. | Other helminths |
|-----------------|-----------|------------------|-----------------|
|                 | Crude     | Adjusted         | Crude           | Adjusted       |
|                 | OR (95% CI) | p value | aOR (95% CI) | p value | OR (95% CI) | p value | aOR (95% CI) | p value |
| ≥100            | 202 (65)   | 1.25 (0.63–2.45) | 1.56 (0.78–3.13) | 0.61 (0.26–1.44) | 0.71 (0.29–1.73) |
| Parent education level |          |                     |                 |                     |                     |                     |                     |
| No or primary education | 244 (79) | 1.00 | 1.00 | 1.00 | 1.00 |
| Secondary/higher education | 66 (21) | 0.57 (0.24–1.36) | 0.53 (0.22–1.28) | 0.60 (0.18–1.97) | 0.63 (0.19–2.09) |
| Parent occupation |          |                     |                 |                     |                     |                     |                     |
| Housewife/unemployed | 196(63) | 1.00 | 1.00 | 1.00 | 1.00 |
| Employed        | 114(37)   | 1.01 (0.52–1.96) | 0.85 (0.42–1.76) | 0.65 (0.25–1.66) | 0.70 (0.26–1.92) |
| Family migration history since child birth |          |                     |                 |                     |                     |                     |                     |
| Migrated        | 23 (7)    | 1.00 | 1.00 | 1.00 | 1.00 |
| Did not migrate | 189 (61)  | 1.58 (0.43–5.84) | 1.55 (0.41–5.80) | 4.74 (1.28–17.63) | 5.30 (1.43–9.74) |
| Unknown         | 98(32)    | 0.74 (0.18–3.09) | 0.74 (0.18–3.10) | 2.24 (0.89–5.63) | 2.04 (0.80–5.18) |

Schistosomiasis includes *S. mansoni* and *S. haematobium* (positive POC-CCA urine cassette test results 1+, 2+, or 3+ and egg-positive urine filtration); other helminth species (based on stool microscopy) include *A. lumbricoides, E. vermicularis*, hookworm, *H. diminuta*, and *S. stercoralis*

1 Past 3 months
2 Hygiene practice: parent/caregiver always wash fruits or vegetables before giving to children
3 US$, United States dollars (1 US$ = 2,190 Tanzanian shillings)

Multivariable mixed logistic regression model with random intercepts at the level of matched pairs, containing the respective variable along with age, sex, and type of toilet

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![Cognitive score by helminth infection](https://doi.org/10.1371/journal.pntd.0006017.g002)

Fig 2. Box-plots comparing development and cognitive function among children with and without helminth infection.

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parameters (MCV, MCH, and RCDW) were equally distributed between helminth-infected and uninfected children.

**Discussion**

We present findings on the prevalence, clinical relevance, and risk factors associated with helminth infection among preschool-aged children in a poorly planned and under-resourced district in the coastal region of Dar es Salaam, Tanzania. We found that the prevalence of *Schistosoma* spp. was high (16.0%) among children under the age of 5 years, but the prevalence of other helminth infections was relatively low. We found no positive associations between helminth infections and commonly reported risk factors or development/cognitive scores. Anemia was a common clinical presentation and more frequent among children infected with helminths than their non-infected counterparts.

To our knowledge, this is the first study to report such a high prevalence of *Schistosoma* spp., as determined by the POC-CCA urine cassette test among preschool-aged children in the coastal urban area of Dar es Salaam. The POC-CCA is considered a highly sensitive rapid diagnostic test and was primarily developed for the detection of *S. mansoni* [20]. In Tanzania, the POC-CCA has previously been used among preschool-aged children to detect *S. mansoni*, reporting a high prevalence of up to 50% in well-known high-risk *S. mansoni* areas around Lake Victoria (North-Western part of Tanzania), where the natural open freshwater serves as a habitat for the intermediate host snails [34, 35]. However, a recent systematic review highlighted a low specificity of the POC-CCA test assay in detecting *S. mansoni* (as compared with stool microscopy) and/or the possibility of cross-reactivity of the assay with *S. haematobium*.

![Box plots showing distribution of hemoglobin and red blood cell indices among children with (n = 73) and without helminth infection (n = 234).](https://doi.org/10.1371/journal.pntd.0006017.g003)
In our study, the positive POC-CCA results were not confirmed by stool microscopy, since the commonly used Kato-Katz method failed to identify any *S. mansoni* eggs in our study population. Furthermore, the urine filtration only revealed a very low prevalence of *S. haematobium* (1.0%). Similarly, in a recent investigation in Dar es Salaam that used Kato-Katz and urine filtration but not the POC-CCA, the prevalence of *S. haematobium* among school-aged children was reported to be 1.2%, while no *S. mansoni* was reported [36]. Likely, the conventional stool and urine examination underestimate the true prevalence due to their low sensitivity to detect light intensity infection as they might occur in young children. However, an overestimation of *Schistosoma* spp. prevalence by a potential cross-reactivity of the POC-CCA with other conditions can also not be fully ruled out [30].

Urban schistosomiasis caused by *S. mansoni* has been reported elsewhere, including Brazil [37], Côte d’Ivoire [38] and Tanzania [39], but most of these studies did not include preschool-aged children. However, intense transmission of *S. mansoni* has never been formally demonstrated in urban regions of Tanzania such as Dar es Salaam [40, 41]. Dar es Salaam is a coastal city along the Indian Ocean and it was known to have a high prevalence and transmission of *S. haematobium* since the 1980s [34, 40]. Our study showed that the prevalence of *S. haematobium* and *S. mansoni* infection as determined by egg counts in urine and stool is low, while the POC-CCA suggests that infections due to *Schistosoma* spp. have a considerably higher prevalence. Further studies using highly sensitive and specific tests for schistosomiasis diagnosis in coastal Tanzania involving different age and population groups should be conducted to establish the species- and age-specific prevalence as the global focus is shifting toward disease elimination.

Overall, the prevalence of other helminth infections was found to be lower than that reported in other under-resourced settings [16, 42]. Ten years ago, a study in two district hospitals in Dar es Salaam reported a soil-transmitted helminth prevalence (including hookworm, *A. lumbricoides*, and *T. trichiura*) of 33% among children below the age of 5 years [43]. The lower rates noted in our study may be due to an improved socioeconomic status among the general population and/or to successful biannual preventive chemotherapy campaigns, initiated in 2004, that include administering mebendazole and vitamin A supplementation to preschool-aged children [44].

We did not find any association between helminth infections and commonly reported risk factors such as age, hygiene, low socioeconomic status, and history of migration. This is in contrast to other studies, which identified age, poor hygiene, and low socioeconomic status as risk factors for helminth infection in children [16, 17, 35, 45]. The lack of association with risk factors might be in part due to our sampling strategy, which was primarily powered to detect the prevalence of helminth infection among our study population, rather than association with risk factors. Although we identified having toilets with septic tanks as a risk factor for *Schistosoma* spp. infection, this association lacked statistical significance after including POC-CCA trace results. We did not find evidence of an association between helminth infection and TB exposure. To our knowledge, no study has yet specifically investigated schistosomiasis and TB in preschool-aged children. However, a study in Kenya reported increased odds of hookworm infection among school-aged children with latent TB infection compared to unexposed controls [6]. It will be important to further elucidate the impact of helminth co-infections in early childhood on developing TB.

We documented a high prevalence of anemia among preschool-aged children that was associated with helminth infection. Similar findings have been reported in studies from Ethiopia and Nigeria, where children who were infected with two or more helminth species were at higher risk of having anemia [46]. High prevalence of anemia among preschool-aged children might also be caused by poor diets, low socioeconomic status of parents or caregivers, as indicated by the high rate of unemployment [23, 47]. Other assessed hematological parameters...
were not associated with helminth infection, possibly due to low prevalence and intensity of helminth infection as well as to the good nutritional status among children evidenced by HAZ and WAZ in our study [48]. Previous research showed that heavy helminth infection impairs development and cognition [10,49]. In our study, helminth infection was not associated with reduced development and cognition. However, such differences may be seen only over longer time frames during detailed follow-up surveys.

Our study has strengths and limitations that warrant further consideration. We systematically screened for helminthiases and other diseases, such as malaria, HIV, and active TB, using a suite of standardized and quality-controlled diagnostic tests [25, 34, 50]. These infectious diseases all contribute to high morbidity and mortality among children <5 years [11]. The main limitations of our study include sampling households based on TB exposure (given that the overall study aim was to explore interactions of TB and helminth co-infections), and restricting the study area to an urban setting. However, poorly planned urban settings have the highest population growth in sub-Saharan Africa with considerable disease burdens of major infectious and non-communicable diseases [51].

In conclusion, our study showed high prevalence of Schistosoma spp. infection as determined by the POC-CCA urine cassette test, among preschool-aged children, even in a highly urbanized setting in East Africa, an observation that has not been previously reported. It must be noted though that this result was achieved with a highly sensitive diagnostic assay, namely, the POC-CCA urine cassette test. Cross-reactivity with other conditions cannot be ruled out. Helminth infections were associated with anemia, but not with growth development and development of cognitive functions among our group of young children. However, the fact that helminth infection was not shown to affect children’s development and cognition does not mean they will not be affected later in life. With the WHO’s ambitious goal of reaching 100% coverage of preventive chemotherapy targeting major helminthiases, our findings call for urgent planning and implementation of specific interventions to prevent further morbidity, and to improve health, care, and wellbeing of these young children. Deworming likely reduces the prevalence of anemia, improves children’s development and cognition, and prevents complications later in life [46, 52]. Future research to confirm our findings using newly developed and highly sensitive and specific test assays, to identify and map Schistosoma spp. infection hotspots and its intermediate host snails in Dar es Salaam are needed to design targeted interventions for effectively controlling morbidity due to schistosomiasis and shift toward interruption of transmission.

Supporting information

S1 Checklist. STROBE checklist.

S1 Table. Additional analysis: Risk factors for S. mansoni infection (defined trace results as positive based on point-of-care circulating cathodic antigen (POC-CCA) urine cassette test) among 310 under-five children in Temeke district, Dar es Salaam, Tanzania.

S2 Table. Comparison of cognitive score among helminth-infected and non-infected preschool-aged children in Dar es Salaam, Tanzania.

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**References**

1. Utzinger J, Becker SL, Knopp S, Blum J, Neumayr AL, Keiser J, et al. Neglected tropical diseases: diagnosis, clinical management, treatment and control. Swiss Med Wkly. 2012; 142:w13727. Epub 2012/11/28. https://doi.org/10.4414/smw.2012.13727 PMID: 23180107.

2. Pullan RL, Smith JL, Jasrasaria R, Brooker SJ. Global numbers of infection and disease burden of soil transmitted helminth infections in 2010. Parasit Vectors. 2014; 7:37. Epub 2014/01/23. https://doi.org/10.1186/1756-3305-7-37 PMID: 24447578; PubMed Central PMCID: PMCPMC3905661.

3. Hotez PJ, Molyneux DH, Fenwick A, Kumareshan J, Ehrlich Sachs S, Sachs JD, et al. Control of neglected tropical diseases. N Engl J Med. 2007; 357:1018–27. Epub 2007/09/07. https://doi.org/10.1056/NEJMra064142 PMID: 17804846.

4. Bartram J, Cairncross S. Hygiene, sanitation, and water: forgotten foundations of health. PLoS Med. 2010; 7:e1000367. Epub 2010/11/19. https://doi.org/10.1371/journal.pmed.1000367 PMID: 21089694; PubMed Central PMCID: PMC2876722.

5. Thomas TA, Mondal D, Noor Z, Liu L, Alam M, Haque R, et al. Malnutrition and helminth infection affect performance of an interferon gamma-release assay. Pediatrics. 2010; 126(6):e1522–9. https://doi.org/10.1542/peds.2010-0885 PMID: 21059723.

6. Sachiy Nagi MI. Relationship between Mycobacterium tuberculosis and hookworm infections among school children in Mbite, Kenya. J Trop Dis. 2013;(03). https://doi.org/10.4172/2329-891X.1000120

7. Mhimbira F, Hella J, Said K, Kwavela L, Sasamalo M, Mara M, et al. Prevalence and clinical relevance of helminth co-infections among tuberculosis patients in urban Tanzania. PLoS Negl Trop Dis. 2017; 11(2):e0005342. Epub 2017/02/09. https://doi.org/10.1371/journal.pntd.0005342 PMID: 28178325.

8. Lustgeman S, Prichard RK, Gazzinelli A, Grant WN, Boatin BA, McCarthy JS, et al. A research agenda for helminth diseases of humans: the problem of helminthiasis. PLoS Negl Trop Dis. 2012; 6(4):e1582.
Jukes MC, Nokes CA, Alcock KJ, Lambo JK, Khiamia C, Ngorosho N, et al. Heavy schistosomiasis.

Albonico M, Allen H, Chitsulo L, Engels D, Gabrielli AF, Savioli L. Controlling soil-transmitted helminthiasis in pre-school-age children through preventive chemotherapy. PLoS Negl Trop Dis. 2008; 2(3):e126. Epub 2008/03/28. https://doi.org/10.1371/journal.pntd.0000126 PMID: 18365031; PubMed Central PMCID: PMCPMC2274864.

Scott SP, Chen-Edinboro LP, Caulfield LE, Murray-Kolb LE. The impact of anemia on child mortality: an updated review. Nutrients. 2014; 6(12):5915–32. Epub 2014/12/24. https://doi.org/10.3390/nu6125915 PMID: 2553005; PubMed Central PMCID: PMCPMC4277007.

Berhe N, Myrvang B, Gundersen SG. Gastro-intestinal symptoms associated with intense Schistosoma mansoni infection affect class-attentionweness of schoolchildren in Ethiopia. Acta Trop. 2009; 110(1):52–6. Epub 2009/03/14. PMID: 19283896.

DiNardo AR, Mace EM, Lesteberg K, Cirillo JD, Mandalakas AM, Graviss EA, et al. Schistosome soluble egg antigen decreases Mycobacterium tuberculosis-specific CD4+ T-Cell effector function with concomitant arrest of macrophage phagolysosome maturation. J Infect Dis. 2016; 214(3):479–88. Epub 2016/07/09. https://doi.org/10.1093/infdis/jiw156 PMID: 27389356; PubMed Central PMCID: PMCPMC4936646.

Tristao-Sa R, Ribeiro-Rodrigues R, Johnson LT, Pereira FE, Dietze R. Intestinal nematodes and pulmonary tuberculosis. Rev Soc Bras Med Trop. 2002; 35(5):533–5. Epub 2003/03/08. PMID: 12621678.

Alemu A, Tegegne Y, Damte D, Melku M. Schistosoma mansoni and soil-transmitted helminths among preschool-aged children in Chuahit, Dembia district, Northwest Ethiopia: prevalence, intensity of infection and associated risk factors. BMC Public Health. 2016; 16:422. Epub 2016/05/25. https://doi.org/10.1186/s12889-016-2864-9 PMID: 27216255; PubMed Central PMCID: PMCPMC4876558.

Davis SM, Worrell CM, Wiegand RE, Odero KO, Suchdev PS, Ruth LJ, et al. Soil-transmitted helminths in pre-school-aged and school-aged children in an urban slum: a cross-sectional study of prevalence, distribution, and associated exposures. Am J Trop Med Hyg. 2014; 91(5):1002–10. https://doi.org/10.4269/ajtmh.14-0060 PMID: 25157123; PubMed Central PMCID: PMCPMC4288685.

WHO. Carter Centre. Intergrated control of the neglected tropical diseases: a neglected opportunity ripe for action. Paper jointly prepared by WHO and the Carter Center presented to the Global Health and the United Nations meeting, May 8, 2008. World Health Organization. 2008.

MoHSW. Strategic Master Plan for the Neglected Tropical Diseases Control Program 2017–2022 Tanzania Mainland. Ministry of Health and Social Welfare. 2017.

Colley DG, Binder S, Campbell C, King CH, Tchuem Tchuente LA, N’Goran EK, et al. A five-country evaluation of a point-of-care circulating cathodic antigen urine assay for the prevalence of Schistosoma mansoni. Am J Trop Med Hyg. 2013; 88(3):426–32. Epub 2013/01/23. https://doi.org/10.4269/ajtmh.12-0639 PMID: 23391918; PubMed Central PMCID: PMCPMC3592520.

MoHSW. Standard Treatment Guidelines and Essential Medicines List (4th Edition). 2013.

NTLP, MoHSW. National Guidelines for the Management of Tuberculosis in Children (1st edition). National Tuberculosis and Leprosy Programme and Ministry of Health and Social Welfare. 2012.

National Bureau of Statistics, Regional Commissioner’s Office. Dar es Salaam Region Socio-economic Profile 2014/2011/.

Grimes DA, Schulz KF. Compared to what? Finding controls for case-control studies. Lancet. 2005; 365:1429–33. Epub 2005/04/20. https://doi.org/10.1016/S0140-6736(05)66379-9 PMID: 15836892.

Mandalakas AM, Kirchner HL, Lombard C, Walzl G, Grewal HM, Gie RP, et al. Well-quantified tuberculosis exposure is a reliable surrogate measure of tuberculosis infection. Int J Tuberc Lung Dis. 2012; 16 (8):1033–9. Epub 2012/06/14. https://doi.org/10.5588/ijtld.12.0027 PMID: 22692027.

Salim N, Schindler T, Abdul U, Rothen J, Genton B, Lweno O, et al. Enterobiasis and strongyloidiasis and associated co-infections and morbidity markers in infants, preschool- and school-aged children from rural coastal Tanzania: a cross-sectional study. BMC Infect Dis. 2014; 14:644. Epub 2014/12/10. https://doi.org/10.1186/s12879-014-0644-7 PMID: 25486986; PubMed Central PMCID: PMCPMC4271451.

Gladstone M, Lancaster GA, Umar E, Nyirenda M, Kayira E, van den Broek NR, et al. The Malawi Development Assessment Tool (MDAT): the creation, validation, and reliability of a tool to assess child development in rural African settings. PLoS Med. 2010; 7(5):e1000273. Epub 2010/06/04. https://doi.org/10.1371/journal.pmed.1000273 PMCID: PMCPMC2964968.
45. Worrell CM, Wiegand RE, Davis SM, Odero KO, Blackstock A, Cuellar VM, et al. A Cross-sectional study of water, sanitation, and hygiene-related risk factors for soil-transmitted helminth infection in urban school- and preschool-aged children in Kibera, Nairobi. PLoS One. 2016; 11(3):e0150744. https://doi.org/10.1371/journal.pone.0150744 PMID: 26950552; PubMed Central PMCID: PMCPMC4780697.

46. Yimam Y, Degarege A, Erko B. Effect of anthelminthic treatment on helminth infection and related anaemia among school-age children in northwestern Ethiopia. BMC Infect Dis. 2016; 16(1):613. Epub 2016/10/30. https://doi.org/10.1186/s12879-016-1956-6 PMID: 27793110; PubMed Central PMCID: PMCPMC5084399.

47. Ministry of Health Community Development Gender Elderly and Children, Ministry of Health, National Bureau of Statistics, Office of the Chief Government Statistician, ICF. Tanzania Demographic and Health Survey and Malaria Indicator Survey (TDHS-MIS) 2015–2016.

48. Erismann S, Knoblauch AM, Diagbouga S, Odermatt P, Gerold J, Shrestha A, et al. Prevalence and risk factors of undernutrition among schoolchildren in the Plateau Central and Centre-Ouest regions of Burkina Faso. Infect Dis Poverty. 2017; 6:17. Epub 2017/01/20. https://doi.org/10.1186/s40249-016-0230-x PMID: 28100278; PubMed Central PMCID: PMCPMC5244543.

49. Yentur Doni N, Yildiz Zeyrek F, Simsek Z, Gurses G, Sahin I. Risk factors and relationship between intestinal parasites and the growth retardation and psychomotor development delays of children in Sanliurfa, Turkey. Turkiye Parazitol Derg. 2015; 39(4):270–6. Epub 2016/01/27. https://doi.org/10.5152/tpd.2015.3620 PMID: 26809913.

50. Graham SM, Ahmed T, Amanullah F, Browning R, Cardenas V, Casenghi M, et al. Evaluation of tuberculosis diagnostics in children: 1. Proposed clinical case definitions for classification of intrathoracic tuberculosis disease. Consensus from an expert panel. J Infect Dis. 2012; 205 Suppl 2:S199–208. Epub 2012/03/27. https://doi.org/10.1093/infdis/jis008 PMID: 22448023; PubMed Central PMCID: PMCPMC3334506.

51. Zaman MM, Bhuiyan MR, Karim MN, Moniruzzaman, Rahman MM, Akanda AW, et al. Clustering of non-communicable diseases risk factors in Bangladeshi adults: An analysis of STEPS survey 2013. BMC Public Health. 2015; 15:659. Epub 2015/07/15. https://doi.org/10.1186/s12889-015-1938-4 PMID: 26169788; PubMed Central PMCID: PMCPMC4501055.

52. Andrews JR, Bogoch II, Utzinger J. The benefits of mass deworming on health outcomes: new evidence synthesis, the debate persists. The Lancet Global health. 2017; 5:e4–e5. Epub 2016/12/14. https://doi.org/10.1016/S2214-109X(16)30333-3 PMID: 27955787.