EEFECT OF PRAZIQUANTEL TREATMENT ON ANTISCHISTOSOME IgE LEVELS IN PRIMARY SCHOOL CHILDREN, WITH SINGLE AND DUAL Schistosoma mansoni AND Schistosoma haematobium INFECTION IN TAVETA SUB COUNTY, KENYA

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ABSTRACT

Background

Helminth infections caused by schistosomes are among the most endemic, communicable diseases of humans who live in parts of the developing world. Integrated strategies for the prevention of worm infections; including regular monitoring of infections, regular deworming and environmental sanitation, have significant impact on child health, growth and cognitive development. Monitoring the immunological effect of treatment for primary school children with single and dual schistosomiasis infection is very critical especially in endemic areas where dual infection is prevalent. This study therefore sought to investigate the significance of treatment on IgE levels before and after treatment with praziquantel among primary school children infected with schistosomiasis.

Methods

The sampling frame included 442 primary school children of both sexes in the county at baseline and eight weeks after treatment. Baseline data on antibody levels was collected before the yearly Kenya National deworming activity. Follow-up data was collected 8 weeks after treatment. Antibody detection and quantification was done by micro ELISA technique. All statistical analyses were conducted in STATA Version 12.0. The Non Parametric Wilcoxon sum rank tests (Mann-Whitney U tests) for the independent samples were performed to compare IgE levels against SEA and SWAP in the periods before and after treatment. A quartile regression was performed to check the relationship of the IgE levels with age.

Results

The average overall IgE levels as measured by optical density decreased from 0.128 to 0.07 after treatment indicating a decrease which suggests a reduction in infection. The IgE levels increased by 0.000875 for every additional increase in the age of the children and the relationship was found to be significant ($P < 0.05$) after treatment.

Conclusions

There were high IgE levels before treatment as compared to eight weeks after treatment. Praziquantel plays an important role by unmasking the tegument of the schistosome worm therefore increasing the antibody antigen reaction. Praziquantel therefore boosts the IgE immune response following treatment.

There was an increase in IgE levels with age.

Key words

*S.mansoni, S.haematobium, IgE, Praziquantel*
1.0 BACKGROUND

Schistosomes can live and mate in the human host without causing any harm and only eliciting immunological reactions when their eggs are trapped in the tissues of the liver or bladder. At this point, strong granuloma T-cell mediated reactions lead to fibrosis in the liver and nodules [1]. The adult worms evade immune attack by covering their surface with antigens derived from host cells, at the same time stimulating antibody which may destroy subsequent infections at an early stage. Eosinophils, macrophages, Immunoglobulin G (IgG) and Immunoglobulin E (IgE) all play a role in host immune defense against schistosomiasis [1]. Schistosomes also secrete a variety of molecules which destroy host antibodies and inhibit macrophages making the destruction of the adult worm impracticable. The combination of adult survival with killing of young forms is referred to as ‘concomitant immunity’ [1].

IgE’s main function is immunity to parasitic helminths [2] like *Schistosoma mansoni*, *Trichinella spiralis*, and *Fasciola hepatica* [3],[4], [5]. Like other immunoglobulin types, IgE is produced by B cells and plasma cells. In contrast to other immunoglobulin types, the concentration of IgE in the circulation is very low [6]. Immunoglobulin E in cord blood usually measures less than 1 U/mL (1 U 5 2.4 ng). Generally, adult IgE levels are achieved by 5 to 7 years of age. Between the ages of 10 and 14 years, IgE levels may be higher than those in adults. After age 70 years, IgE levels may decline slightly and be lower than the levels observed in adults younger than 40 years [6]. Circulating IgE concentrations are very low because mast cells have a very high affinity for IgE (1010 mol/L21) via their e-heavy-chain Fc receptors (FceR). The synthetic rate for IgE is also very low. Immunoglobulin E attaches to mast cells and to basophils and activated eosinophils [6].

Immunoglobulin E (IgE) plays a vital role in host immune protection against parasites. The role of IgE was first found by studies carried out on the cell mediated killing of schistosomes, as well as by epidemiological surveys in areas with endemic schistosomiasis [7]. Studies showed that after the first 4-5 weeks of exposure to cercariae when host immune system is aimed at worm antigens, the immune response is primarily Th1 in nature. During normal infection after eggs of schistosomes are produced, the immune response becomes highly Th2-polarized and after this the development of Th2 response follows. At this stage, there are increases in both plasma IgE levels and the number of circulating eosinophils, which mirror the production of Interlukin 4 (IL-4) and Interlukin 5 (IL-5). These are the key cytokines of Th2 cells that assist in class switching of B cells to IgE isotype and play the role of growth and survival factor for eosinophils, respectively [8].

Past studies have shown that resistance to reinfection may be due to the protective effect of IgE against adult schistosome antigens [9]. Antibodies of IgE isotype play a major role in protection against schistosomiasis by macrophage mediated toxicity. Experiments have also shown that eosinophils can destroy *S. mansoni* in the presence of specific IgE antibodies [10]. Th2 cells express Cytokines and CD4 ligands that stimulate B lymphocytes to express specific antibodies called IgE. IgE operates as an opsonizing antibody that attaches phagocytic eosinophils to helminthic worms and permit the release of major basic proteins. IgE also enables eosinophil cationic proteins to be focused on the targets for extracellular destruction of the helminthes. The Fab portion of IgE identifies epitopes on the helminth worm, whereas the Fc portion attaches to Fc receptors of activated eosinophils. The lysosomal proteases of eosinophils are able to tear down the tough integument of helminth worms. IgE also promotes inflammation to recruit phagocytic cells [10].
Praziquantel is the most effective chemotherapeutic agent against schistosomiasis and has also been found to work in synergy with host immune response. Past studies have established that Praziquantel can destroy adult worms’ in tegument, stimulate flaccid paralysis of worms and expose internal antigens [11]. Human host humoral and cellular immune responses can be activated after exposure to these worm antigens. Studies have been conducted to establish the development of humoral response after treatment with schistosomiasis infection [12]. A study conducted among 57 children aged between 6-15 years old in eastern Zimbabwe, established that production of IgA and IgG2 was remarkably lower after treatment compared to before treatment [12]. This finding can be accredited to the fact that these antibodies are aimed at the glycanic antigens on the tegument of adult worms. It was noted that after treatment these antigens disappeared and the amount of IgA and IgG2 declined. On the other hand, the levels of IgE, IgG1 and IgG4 against SEA were significantly higher in post-treatment than the pre-treatment follow ups [12]. A study in Kenya on changes of human isotype responses to S. mansoni antigens following treatment indicated that no significant differences were observed between pre-treatment and post treatment isotype responses to egg antigens [13]. The study also showed that IgG subclass responses to adult worm antigens were considerably lower after treatment, while IgE levels against adult worm antigens were significantly higher after treatment than before treatment. Similar phenomena were observed in another study in which antischistosomular tegument IgG4 considerably decreased and anti-Schistosomular tegument (STEG) and anti-soluble worm antigen preparation (SWAP) IgE increased after treatment in a population that displayed resistance to reinfection. The resistant group was significantly older than the group susceptible to reinfection [14] indicating, immunity to reinfection with increasing age.

A recent study in Kenya, conducted in a highly endemic area of the Lake Victoria region, Asembo bay, found that some children exhibited a phenotype indicative of resistance to S. mansoni reinfection by 8–10 years of age [15]. It has been established that infections with schistosomiasis in the lakeside communities begin very early in life [16]. Some of the 8–10-year-old children in the lake Victoria-asembo study could have been infected as early as at age 1 by the time of their enrolment therefore allowing for an opportunity for them to have already experienced dying worms. The resistant phenotype was characterized by high schistosome-specific IgE levels and elevated levels of CD23+ B cells [16]. Repeated Praziquantel treatment of more predisposed children increases these immune responses toward protective levels [15]. Research evidence proves that treatment of school children and adults with praziquantel boosts immune responses associated with resistance to reinfection with schistosomes in endemic areas [12]; [17].

More recent studies have shown that treatment with Praziquantel has enhanced immune response quantitatively and qualitatively. A study conducted in an endemic area in Mashonaland East Province of Zimbabwe, showed that six weeks after treatment, all of the treated children were schistosome egg negative. It was further observed that adult worm and egg-specific IgE titers increased significantly following treatment [18]. Other similar studies have showed that Praziquantel treatment boosts the anti-worm IgE immune responses associated with protection in older individuals [15]. This suggests that the 3-5 age groups may equally gain immunologically from Praziquantel, which reduces reinfection in older children and adults by stimulating IgE responses [17]; [15].
2.0 METHODS

2.1 Study area

This study was conducted in Taveta Sub County. Taveta Sub County is located in Taita Taveta County in the Coastal region of Kenya. It covers an area of 17,084.1 sq Km. The county experiences mean annual rainfall of 650 mm per annum with temperatures averaging 23°C. It has water resources such as Lake Chala, Lake Jipe and Mzima springs that supply the coastal region with water (www.maplandia.com). The site was selected because of the unique prevalence of both S.mansoni and S.haematobium infection, among the population especially in the primary school children [19]. The study area is endowed with water sources, which could be responsible for transmission with schistosomiasis. In Kiwalwa area there is a river Kiwalwa that boarders the school, the community around this area has constructed a canal that is right at the schools perimeter fence which is used for irrigation. Abori area in itself is a swamp, and the area experiences flooding during heavy rains. As one heads to Eldoro there is a river called Abori. At the Kenya –Tanzania boarder there is a river as you head to Lotima called River Nyumba ya Mungu as shown in Figure 1.

2.2 Study population

The study population comprised of 442 primary school children. The school children were aged between 5-16 years, from four primary schools namely, Lotima, Kiwalwa, Abori and Eldoro. The Sub County was purposively sampled owing to the endemicity of helminthic infections.

2.3 Study design

Selected schools were visited 3 months prior to the survey date in order to have the purpose of the survey explained to the head teacher and class teachers concerned. Two levels of consent were sought, according to the sample population. School-level consent was sought from county officer in charge of education and thereafter from the School’s headmaster. Since the national deworming is an ongoing programme, the parents and guardians were already aware of the planned activities as information had already been provided. They were called for a meeting where they were given the chance to ask questions. They were further assured that participation of their children in the study was completely voluntary, and that they had the right to withdraw their children from the study at any time, should they wish to do so.

Pupils from class 1-6 were selected from both sexes using computer generated numbers in a process where each child stood a chance of being selected. For each school, the selection exercise for children took place in the morning while the pupils were in the assembly. The selected children were put in a separate class rooms as the rest of the pupils were released to go to their respective classes to continue with their normal class schedule and lessons. Randomly selected children who declined to take part in the study were not subjected to any duress, but were instead automatically replaced.
2.4 Blood Collection

Children were asked to provide a finger-prick blood sample which was used to collect dry blood spot on Whatman filter paper. Commercially available Whatman filter paper no. 903 circular in shape having a diameter of 125 mm was used for blood sample collection (WHO Memorandum, 1974). Blood was collected as a spot on filter paper near its circumference by finger prick. After explaining the procedure to the school children and their parents and guardians, blood spots were taken from consenting pupils. While taking aseptic precautions, blood was allowed to make a spot on filter paper by touching the filter paper at the site where prick was made. The filter paper was allowed to dry at room temperature for 45 min. After drying, each filter paper was kept in a zip lock paper bag containing desiccant and kept in a cooler box for transportation. In the laboratory the blood spots were stored in a freezer at -20°C awaiting the laboratory procedure.

2.4.1 Determination of antibody responses

The antibody detection and quantification was done using the Enzyme Linked Immunoabsorbent Assay (ELISA) technique (Rujeni et al., 2013). Slight modifications were done after optimization and standardization. In this technique, antigens are loaded on a plate. An antibody conjugated to an enzyme is added. Binding of antibody and antigen is detected by adding a substrate whose break down products after enzymatic reactions give color. This color is detected by ELISA reader.

Before the ELISA procedure the blood spot was punched out with the help of 10 mm paper punch. The punched filter paper was placed in a test tube and eluted with 250µl of Phosphate Buffered Saline with Tween 20 (PBST) at 4°C for 24 hours. After 24 hours the test tube was gently vortexed for proper mixing. The eluted sample was used for *Schistosoma* serology using ELISA.

2.4.2 Method for ELISA

Wells of microtiter plates (Nunc Thermoscientific) were coated with 50ul/well of Soluble Egg Antigen (SEA) at 10µg/ml and 50ul/well of Soluble Worm Antigen (SWAP) 10 µg/ml in Phosphate Buffered Saline (PBS) 1x and incubated overnight at 4°C. The plates were washed the following day 3 times with PBST and banged on a paper towel. The plates were then blocked with 100 µl/well of 3% Phosphate Buffered Saline – Bovine Serum Albumin (PBS-BSA) then incubated at 37°C for 1 hour. The plates were then washed 6 times with PBST. Eluted samples were then loaded into the plates in duplicate at 50ul/well at 1ug/ml and incubated for 2 hours at 37 °C. After incubation the plates were then washed 6 times with Phosphate Buffered Saline Tween (PBST). 50ul/well of Goat antihuman IgE Horseradish Peroxidase (HRP) conjugated antibody was added and incubated for 1 hour at 37 °C. After incubation 150ul/well of 1 step 2,2’-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) were added to the plate, covered with a foil an placed in the dark for color change to develop.

All samples were assayed in duplicate; sera from positive children with schistosome infection were used as positive control while negative sera from volunteers in a non-endemic area were used as negative control. Ige Levels were expressed as optical densities. Optical densities greater than 0.01 were considered as positive IgE levels. The color was allowed to develop in the dark for 30 minutes. Absorbance was then read using an ELISA reader (Biotek) at 630nm.
2.5 Data Management and Analysis

2.5.1 Data collection
This was done before the yearly Kenya National Governments’ primary school deworming programme. During deworming, all the primary school children in Taveta Sub County are treated with a single dose of 40 mg/kg of praziquantel for schistosomiasis and another single dose of albendazole at 400mg/kg for soil transmitted helminth infections. After treatment data was collected from the same children eight weeks later.

2.5.2 Data entry and storage
Data was collected on paper form, counter-checked for accuracy, and verified before double entry into a computer Excel 2007 spreadsheet. All statistical analysis was survey set and carried out using STATA version 12.0. All data does not contain recognizable names for confidentiality.

2.5.3 Data analysis
The nonparametric Wilcoxon sum rank tests (Mann-Whitney U tests) for the independent samples were performed to compare before and after treatment antibody- antigen reaction optical densities (OD). A quartile regression was performed to check the relationship of the optical densities and age. The test was conducted for two antigens namely SEA and SWAP. All statistical analyses were conducted in STATA 12 and P values of <0.05 were considered significant.

3.0 RESULTS

3.1 Demographic Characteristics
Data was collected from 442 children in the study area. The children had an almost equal representation in gender with the majority 227 (51.35%) being female and the male being 215(48.65%). Most 219 (49.15%) of the children surveyed were in age group of 8-10 years with the mean age of 9 years (SD ±0.09 yrs) and ranging from 5-16 years.

3.2 The IgE profile in the school going children infected with schistosomiasis at baseline and after treatment.

General view of IgE levels at baseline and after treatment
From Table 1 below it is evident that the change in OD level of IgE were higher before treatment as compared to after treatment of the primary school children. The mean IgE OD values for SEA was 0.128 before treatment and 0.073 after treatment.

3.4.2 Comparison of IgE levels at baseline and after treatment
Out of the (49/442) infected with S. mansoni before treatment only five were infected after treatment. The cases were positive for S. mansoni before treatment and after treatment. The children recorded IgE OD levels of 0.0833 and 0.0674 in the period before treatment and after treatment with praziquantel respectively as seen in Table 2 below. The reduction in IgE level was significant.
Out of (103/442) children infected with *S. haematobium* 57 were followed up. Four of the followed up children reported infections after treatment and they recorded the following ODs. Higher IgE level were recorded in the four children that tested positive for *S. haematobium* eight weeks after treatment with praziquantel. As seen in Table 3 the IgE OD level was 0.176 and 0.072 in the period before treatment and after treatment respectively.

None of the children who had dual infection before treatment tested positive for either *S. mansoni* or *S. haematobium*. The IgE levels showed a remarkable decrease, the mean IgE titers decreased significantly (p<0.0001) from 0.118 ± 0.098 to 0.068± 0.002 for SEA while for SWAP there was an increase in the period after treatment 0.52 ±0.00408 to 0.064±0.0122.

**Relationship between IgE antibody level with age among the primary school children infected with schistosomiasis**

**IgE profiles in relation to gender and Age**
The overall IgE profile against SEA antigen was significantly higher before treatment as compared to after treatment. As seen in Table 4 below, the mean IgE OD level was 0.128 before treatment and 0.073 after treatment with praziquantel.

When comparing with gender, there was not so much significant difference observed in the IgE levels. For the female pupils, the IgE OD level was 0.133 before treatment and 0.079 after treatment with praziquantel, while for the male pupils it was 0.123 and 0.066 respectively.

In terms of age there was significant change in the IgE levels, across all age groups, levels decreases significantly after treatment as seen in Table 4 below. In the period after treatment the IgE OD levels increased from 0.063 at age group 5-7 years to 0.091 at age group 11-13 years.

The overall IgE profile against SWAP antigen was higher after treatment as compared to before treatment. As seen in Table 3-36 below, the mean IgE OD level was of 0.065 before treatment and 0.071 after treatment with praziquantel.

When comparing with gender, there was significant difference observed in the IgE levels. For the female pupils, the IgE OD level was 0.064 before treatment and 0.078 after treatment with praziquantel. For the male pupils it reduced slightly, where it was 0.065 before treatment and 0.064 after treatment respectively.

In terms of age there was change in the IgE levels. In most of the age groups, levels increased slightly after treatment as seen in Table 5 below. In the period after treatment the IgE values decreased from OD of 0.070 at age group 5-7 years to 0.067 at age group 11-13 years.
Quartile regression of IgE in relation to age

A quartile regression analysis was performed to study further the relationship between IgE and age. It was observed that there was an increase in IgE level with age as seen in Table 6 below. The IgE OD level increased by 0.000875 against SEA for every additional increase in the age of the children and the relationship is significant (P- 0.015) after the treatment.

Likewise for SWAP antigen, there as an increase in IgE level with age in the period after treatment with praziquantel. As seen in Table 6 there was a significant (P 0.034) increase in IgE level against SWAP, which increased by 0.001 units for every additional one year increase in age of the children after treatment.

DISCUSSION

Adult worms, inhabiting human host’s ‘seems’ to be impervious to immune attack. Various means are likely to be accountable for the long-term survival of worm in what is perceived to be a hostile immune surrounding. Some of the means of survival may be attributed to the ability of schistosomes to continually renew its outer tegument through unique somatic stem cells [20] or by acquiring host antigens [21]; [22]. Other facets of their survival may also involve manipulation of and by the host's immune responses, such as isotypic shifts in antibody specificities [23]; [24] and immune regulation. Although schistosome worms inhabit the human body without immediate grave morbidity, an immune response is always mounted, as the host immune system recognizes the schistosome worm and eggs as foreign.

In this current study, the primary school children displayed high IgE levels before treatment as compared to the period after treatment. Treatment with Praziquantel plays an important role in establishing and maintaining immune response during and after infection. Successful treatment of schistosomiasis with Praziquantel depends on having established immune mechanisms that can kill the worms if they have undergone sufficient surface damage after the paralysis caused by the drug [25]; [26]; [27]. It was worth noting that there was an inverse relationship between SEA and SWAP antigens in this study. IgE immune responses against SEA were observed to be high in the period before treatment and showed a decrease after treatment, whereas responses for soluble worm antigen were seen to invariably increase in the period after treatment. In spite of the community in which schistosome immune studies are conducted, there is a prevailing degree of difference in the pattern of immune responses against soluble worm antigens against soluble egg antigens [28]. In a majority of studies, this is observed as high-level responses of individuals with premature infections to soluble egg antigens that then decrease as infections become chronic [29]; [30]; [31]; [32]; [33]; [34]. Responses to soluble worm antigenic preparations (SWAP), in contrast, remain consistently high during early infection and continue to be expressed all through the chronic infections. It is also important to distinguish the history of people being studied beyond current infection with schistosomiasis by taking into consideration how long they have been infected [15], whether the mothers of current children under study were infected during pregnancy [35]; [36]. Another important factor to consider is whether the study subject had been treated with praziquantel and how often [37]; [38]; [39]; [15]. There is a likely possibility that these factors could contribute to the current immune status of the child.
In this current study, re infection after treatment was also observed in *S. haematobium* infection. A higher IgE level was recorded in four children that tested positive for *S. haematobium* before and eight weeks after treatment with Praziquantel. The IgE level was 0.1766 before treatment and 0.072 after treatment. Interestingly none of the children who had dual infection before treatment tested positive for either *S. mansoni* or *S. haematobium*. This signifies that Praziquantel is efficient in clearing dual infection in an individual. It also eliminates the double burden of disease in the children who had tested positive for dual infection. The IgE profile showed a remarkable decrease, the mean IgE levels decreased significantly (p-value<0.0001) from 0.118 to 0.068. This change in IgE levels indicates that the antigen in this case the Schistosome was significantly reduced therefore reducing antibody antigen reaction hence a low production of the antibody (IgE).

Other studies have shown that following treatment of adults, the adult worm-specific IgE levels either increases or is maintained at pretreatment levels. In children, who are more likely to become reinfected, treatment is less likely to increase the level of IgE/IgG4 ratio, an indication that IgE levels would be maintained or remain reduce. Recent studies have shown that, certain *S. mansoni* adult worm-associated tegumental-allergen-like (TAL) proteins have been identified as important potential targets of protective IgE and reinfection-associated IgG4[23]; [40]; [41].

Typical age-infection curves are normally observed in communities endemic with schistosomiasis, showing infection intensities to be high in early adolescence and to decline as age increases. This pattern is thought to be due to acquired immunity to infection. In support of this, IgE antibody levels to worm antigens, which have been linked to resistance to reinfection [14]; [41]; [42]; [43]; [44]; [40] tend to increase with age, whereas antibody levels to egg antigens generally decline or are unchanged [13]; [45].

In this current study, it was observed that there was an increase to IgE levels with age. The IgE levels increased from 0.124 at age group 5-7 to 0.134 at age group 8-10. A similar situation was also observed after treatment with praziquantel, where the IgE levels increased from 0.063 at age group 5-7 to 0.07 at age group 8-10. Other similar studies have showed that, praziquantel treatment boosts the anti-worm IgE immune responses associated with protection in older individuals [15]. This suggests that the 3-5 years age groups may equally gain immunologically from praziquantel, which reduces reinfection in older children and adults by stimulating IgE responses [17], [15].

For both *S. mansoni* and *S. haematobium* responses directed against egg antigen, levels of IgE have been shown to increase with age [46], [43] [42], [32], [47], [48], [13]. Immune responses are believed to develop slowly and to be short lived [49], so that as the hosts age, their cumulative experience of parasite antigens increases, resulting in an increase in acquired resistance. This explanation is supported by both experimental [50] and field studies [51], [52]. The study showed that treatment altered the relationship between the level of antibody produced and age for the isotypes IgE, IgM, IgG1 and IgG2. In all isotypes pretreatment antibody levels increased with age. This is partly expected in this age-group where exposure to infective water also increases with age, so that the increase in antibody levels is attributed partly to increased exposure to parasite antigens [51].
In this current study, the IgE level increased by 0.000875 against SEA for every additional increase in the age of the children after treatment. Likewise, for SWAP antigen, there was an increase in IgE level by 0.001 for every one-year increase in the children with age after treatment with Praziquantel. More recent studies have shown that treatment with Praziquantel has enhanced immune response quantitatively and qualitatively. A study conducted in an endemic area in Mashonaland East Province of Zimbabwe, showed that six weeks after treatment all of the treated children were schistosome egg negative. It was further observed that adult worm and egg-specific IgE titers increased significantly following treatment [18].

REFERENCES


Figures and Tables

Figure 1: Map of the study area
Table 1: Summary statistics IgE values of before and eight weeks after treatment, for two antigens

<table>
<thead>
<tr>
<th></th>
<th>SEA Before treatment</th>
<th>SEA After treatment</th>
<th>SWAP Before treatment</th>
<th>SWAP After treatment</th>
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<tbody>
<tr>
<td>Min</td>
<td>0.0415</td>
<td>0.041</td>
<td>0.04075</td>
<td>0.038</td>
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<tr>
<td>Median</td>
<td>0.0685</td>
<td>0.61</td>
<td>0.05975</td>
<td>0.58</td>
</tr>
<tr>
<td>Mean</td>
<td>0.128</td>
<td>0.073</td>
<td>0.0651</td>
<td>0.0719</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>0.106</td>
<td>0.059</td>
<td>0.0265</td>
<td>0.063</td>
</tr>
<tr>
<td>Skew</td>
<td>1.351</td>
<td>4.8</td>
<td>7.36</td>
<td>5.011</td>
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<tr>
<td>Maximum</td>
<td>0.5945</td>
<td>0.49</td>
<td>0.4155</td>
<td>0.51</td>
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Table 2: IgE levels for positive *S. mansoni* individuals before and after treatment

<table>
<thead>
<tr>
<th></th>
<th>Before treatment</th>
<th>After treatment</th>
<th>(H_a) mean(B.T&gt;A.T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEA</td>
<td>0.0833±0.065</td>
<td>0.0674±0.026</td>
<td>p-value=0.0423</td>
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<tr>
<td>SWAP</td>
<td>0.0638±0.026</td>
<td>0.0652±0.017</td>
<td>p-value=0.3775</td>
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Table 3: IgE levels for positive *S. haematobium* individuals before and after treatment

<table>
<thead>
<tr>
<th></th>
<th>Before treatment</th>
<th>After treatment</th>
<th>(H_a) mean(B.T&gt;A.T)</th>
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<tr>
<td>SEA</td>
<td>0.1766±0.119</td>
<td>0.072±0.054</td>
<td>p-value=0.0000</td>
</tr>
<tr>
<td>SWAP</td>
<td>0.0600±0.116</td>
<td>0.070±0.062</td>
<td>p-value=0.2365</td>
</tr>
</tbody>
</table>

*\(H_a\)* - Alternative Hypothesis
*B.T* – Mean before Treatment
*A.T* - Mean after Treatment

Where \(H_a: B.T>A.T\) Mean before treatment should be greater than mean after treatment

Table 4: IgE levels against SEA displayed across gender and age.

<table>
<thead>
<tr>
<th></th>
<th>Before treatment (mean±SEM)</th>
<th>After treatment (mean±SEM)</th>
<th>Z and P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall 442</td>
<td>0.128±0.106</td>
<td>0.073±0.059</td>
<td>Z=6.56, p=0.0000</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Female 215</td>
<td>0.133±0.108</td>
<td>0.079±0.0075</td>
<td>Z=5.61, p=0.000</td>
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<tr>
<td>Male 227</td>
<td>0.123±0.103</td>
<td>0.066±0.340</td>
<td>Z=3.54, p=0.0004</td>
</tr>
<tr>
<td>Age categories</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-7yrs 106</td>
<td>0.124±0.116</td>
<td>0.063±0.033</td>
<td>Z=2.65, p=0.008</td>
</tr>
<tr>
<td>8-10yrs 219</td>
<td>0.134±0.106</td>
<td>0.070±0.049</td>
<td>Z=5.71, p=0.0000</td>
</tr>
<tr>
<td>11-13yrs 112</td>
<td>0.121±0.094</td>
<td>0.091±0.091</td>
<td>Z=1.96, p=0.0496</td>
</tr>
<tr>
<td>&gt;13yrs 5</td>
<td>0.127±0.094</td>
<td>0.058±0.013</td>
<td>Z=0.94, p=0.3472</td>
</tr>
</tbody>
</table>
Table 5: IgE levels against SWAP displayed across gender and age.

<table>
<thead>
<tr>
<th></th>
<th>Before treatment (mean ±SEM)</th>
<th>After treatment (mean ±SEM)</th>
<th>Z and P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall</strong></td>
<td>0.065±0.0265</td>
<td>0.071±0.063</td>
<td><strong>Z=3.26, P=0.0011</strong></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.064±0.020</td>
<td>0.078±0.083</td>
<td><strong>Z=2.87, P=0.0004</strong></td>
</tr>
<tr>
<td>Male</td>
<td>0.065±0.031</td>
<td>0.064±0.028</td>
<td><strong>Z=1.69, P=0.09</strong></td>
</tr>
<tr>
<td><strong>Age categories</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-7yrs</td>
<td>0.070±0.045</td>
<td>0.067±0.059</td>
<td><strong>Z=3.34, P=0.0008</strong></td>
</tr>
<tr>
<td>8-10yrs</td>
<td>0.062±0.015</td>
<td>0.070±0.062</td>
<td><strong>Z=2.06, P=0.0389</strong></td>
</tr>
<tr>
<td>11-13yrs</td>
<td>0.065±0.015</td>
<td>0.080±0.073</td>
<td><strong>Z=0.43, P=0.6671</strong></td>
</tr>
<tr>
<td>&gt;13yrs</td>
<td>0.058±0.020</td>
<td>0.065±0.012</td>
<td><strong>Z=0.94, P=0.3472</strong></td>
</tr>
</tbody>
</table>

Table 6: Quartile regression of IgE in relation to age.

<table>
<thead>
<tr>
<th>IgE</th>
<th>Age(co-efficient and p-values)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
</tr>
<tr>
<td>SEA</td>
<td>0.000375(p-value=0.792)</td>
</tr>
<tr>
<td>SWAP</td>
<td>0.00025(p-value=0.541)</td>
</tr>
</tbody>
</table>

DECLARATIONS

ETHICS APPROVAL AND CONSENT TO PARTICIPATE
Consent to conduct this study was granted by the Kenya Medical Research Institute, Scientific Review Unit. Protocol number SSC 2872

CONSENT FOR PUBLICATION
The Kenya national deworming programme is an ongoing yearly activity that has been taking place for more than 8 years. Before the programme begun, the parents, teachers, school administration from county governments in endemic areas were informed of the programme. Before every exercise in this study, meetings were held with the county government of Taveta, department of education, the teachers and the local district hospital, to inform them about the exercise. Parents and guardians gave permission for their children to take place in the study and they had the chance to ask questions and were informed that participation of their children in the study was completely voluntary and that they had the right to withdraw from the study at any time.

AVAILABILITY OF DATA AND MATERIAL
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.
COMPETING INTERESTS
The authors declare that they have no competing interests

FUNDING
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WT Principal Supervisor
CM Lead researcher KEMRI
DY Supervisor Technical University
AM Supervisor University of Nairobi
LN Statistician
IW assisted in editing manual
All authors read and approved the final version of the manuscript

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