

## Prevalence of enteroparasitic infections and related hormonal and immunological repercussions that may compromise students' physical performance

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**Abstract.** The aim of this study was to evaluate the prevalence of enteroparasitic infections in students and their hormonal and immunological repercussions on physical development. Students of basic education of both sexes were evaluated. Parasitological stool tests were performed using the Hoffman and Kato-Katz methods. The students were divided into two groups: a control group (negative parasitological examination, N=25) and an infected group (positive parasitological test, N=25). Anthropometric variables (height, weight, and BMI), concentrations of hormones (melatonin and cortisol), cytokine/chemokine levels (IL-1 $\beta$ , IL-6, IL-8, IL-10, IL-12, IL-17 and TNF- $\alpha$ ) and physical performance (aerobic capacity, upper- and lower-limb muscle strength and abdominal performance) were evaluated. The prevalence of parasitic infection among the students was 7.98%. No anthropometric differences were observed among the groups. IL-2 and TNF- $\alpha$  levels were higher and IL-8 levels were lower in serum from students who were positive for parasitic infection. Serum from students who were positive for parasitic infection showed higher levels of melatonin than that from parasite-negative students. No differences were observed in cortisol levels. Students who were positive for parasitic infection presented greater lower-limb strength and lower abdominal performance than parasite-negative students. In the parasitic infection group, IL-12 was positively correlated with melatonin. In the parasitic infection group, IL-8 showed a positive correlation with aerobic capacity, while IL-17 and TNF- $\alpha$  showed a positive correlation with abdominal performance. These data suggest that parasitic infections determine the profile of inflammatory cytokines and that melatonin may be involved in the control of this process to minimize tissue damage. Additionally, students' difficulty in practising physical exercises can be an indication of enteroparasitic infection.

### INTRODUCTION

Despite advances in the control of infant morbidity and mortality and in basic care, there are still several health problems in practically all urban areas of Brazil, with greater intensity among the vulnerable populations of the peripheral territories. The lack of infrastructure increases the epidemiological complexity, favouring the emergence of new diseases and the

resurgence of old endemics, including parasitic infections (Hijjar *et al.*, 2005).

Weight-height deficit and anaemia are the main causes of morbidities associated with childhood enteroparasitic infections. Parasitic infections may compromise nutritional status due to reduced food intake and/or increased nutrient loss (Ostan *et al.*, 2007; Araújo Filho *et al.*, 2011). Thus, helminth and protozoal infections have been associated with a number of adverse

health consequences, including inadequate growth and decreased physical performance (Lander *et al.*, 2012).

Physical exercise causes functional changes in the immune system and may induce an inflammatory response by increasing serum levels of IL-1, TNF- $\alpha$  and IL-6, followed by the release of anti-inflammatory cytokines, such as IL-10. The type, duration and intensity of exercise greatly influence the post-exercise cytokine response profile. The release of IL-1 appears to be most sensitive to exercise intensity, whereas TNF- $\alpha$  and IL-6 are most sensitive to exercise duration (Ferreira, 2009).

The cytokine IL-6, along with the cytokines IL-1, IL-4, IL-5, IL-10 and IL-13, seems to determine the pattern of inflammatory responses, increased antibody production and marked eosinophil activation (Gleeson, 2006). Inflammation is considered a highly beneficial and necessary process in regular and systematized physical training because, in conjunction with the action of hormones, it is responsible for the regeneration and repair of damaged structures (Zaldivar *et al.*, 2006).

The hormones cortisol (produced by the adrenal gland) and melatonin (secreted by the pineal gland) have been reported to act on immune mechanisms involved in the parasite-host relationship, especially during parasitic infections. These hormones can modulate the immune response profile, as the levels of these hormones modulate cytokine production (Martinez-Bakker *et al.*, 2015; Quintanar-Stephano *et al.*, 2015).

Melatonin can influence both humoral and cellular responses as well as the production of mediators. The actions of this hormone have been related to several pathologies, including infections and inflammation (Carrillo-Vico *et al.*, 2004; Santello *et al.*, 2007; Santello *et al.*, 2008a; Santello *et al.*, 2008b). However, the effects of this hormone on individuals who practise physical exercise are still only partially understood.

However, there is controversy in the literature on the influence of enteroparasitic infections on physical aptitude. Some authors report that children with parasitic infection

are strongly affected (Yap *et al.*, 2012) and that diarrhoea caused by helminth infection influences the development of physical aptitude (Guerrant *et al.*, 1999). Additionally, after treatment, there is an improvement in physical capacity (Stephenson *et al.*, 1990; Stephenson *et al.*, 1993). However, other studies suggest that enteroparasitic infections do not influence physical activity (Muller *et al.*, 2011).

However, no data have been found in the literature demonstrating that enteroparasitic infections can influence physical performance through effects on hormones and cytokines. Considering that parasitic infections in organisms can cause several neuroimmunoendocrine alterations, the aim of this study was to evaluate the prevalence of enteroparasitic infections and their possible hormonal and immunological repercussions on the physical development of students.

## MATERIALS AND METHODS

The prevalence and load of enteroparasites among students and the correlations among anthropometric measures and immunological and hormonal factors were evaluated in a cross-sectional study.

This study was approved by the Federal University of Minas Gerais Research Ethics Committee (CAAE 19354513.3.0000.5149), and parents or legal guardians gave informed written consent before of students participating in the experiment.

### Subjects

The study was carried out on a population composed of elementary school students of both sexes aged 5 to 14 years with medium age of 9,7 years and enrolled in public educational institutions of the municipality of Jaboticatubas, MG, Brazil. Among the basic sanitation conditions of the students, only 13.2% had a sewage system, but without treatment. The majority declared to use a septic tank for domestic sewage (73.6%) and were supplied by a public treated water network (63.3%). The disposal of household waste was the municipal responsibility

(52.8%); and 41.5% of students affirm to bury or burn household waste.

The population of elementary school students aged 5 to 14 years in Jaboticatubas is 1,294 individuals. According to the sample calculation by the OpenEpi2 program (Version 2.3.1, with a 95% confidence level), the minimum sample number for the study was 207 children, but in this study, 313 children were initially examined. Subjects within the defined age range were randomly selected. The students were submitted to parasitological exams of faeces, and 25 (13 female and 12 male) of a total of 313 students had parasitic infection.

After parasitological evaluation, 25 students (13 female and 12 male) with negative parasitological examination were randomly chosen to compose the control group. Thus, the students were divided into two groups, the control group (negative parasitological examination, N=25) and the infected group (positive parasitological test, N = 25), for quantification of hormones and cytokines and evaluation of physical performance. After performing the physical tests and undergoing blood collection, all infected students were referred for specific treatment.

### **Inclusion and Exclusion Criteria**

The inclusion criteria were as follows: (a) age of 5-14 years; (b) school children enrolled in the public school system; (c) signed a consent form and (d) not using any antiparasitic agents during the collection period for faecal material and blood samples. School children who presented cognitive, psychiatric or behavioural disorders were excluded.

### **Stool examination**

For stool collection, glass containers that had been previously labelled with the name, age and grade of each student were distributed to the participants the day before collection. The samples were collected the next day. Stool samples were subjected to two methods: the spontaneous sedimentation method (Hoffman *et al.*, 1934) and the Kato-Katz Method (Katz *et al.*, 1972) using a Helm

Test Kit (Bio Manguinhos, Fiocruz, Rio de Janeiro, Brazil).

### **Blood sampling**

Blood samples were always taken in the morning. Blood (10 mL) was collected from each subject in tubes without anticoagulant. We centrifuged the blood samples at 300×g for 15 min until serum separation. Serum samples were stored individually in aliquots of 500 µL at -80°C for further analysis.

### **Melatonin determination by the immuno-enzymatic method**

Melatonin was extracted from serum by affinity chromatography, concentrated in speed vacuum and measured with a commercial ELISA kit (IBL, Hamburg, Germany). The concentration was measured by absorbance in a spectrophotometer equipped with a plate-reader and 405 nm filter. Melatonin levels were calculated based on the standard curve in pg/mL.

### **Cortisol determination by the immuno-enzymatic method**

Cortisol levels were determined from serum using a commercial ELISA kit (Accu Bind ELISA kit, IBL, Hamburg, Germany). The concentration was measured by absorbance in a spectrophotometer with a 405 nm filter. Cortisol levels were calculated based on the standard curve in µg/dL.

### **Quantification of cytokines**

Blood samples were collected, and the serum obtained was stored at -80°C prior to analyses. The samples were thawed, and cytokines (IL-1β, IL-6, IL-8, IL-10, IL-12, IL-17 and TNF-α) were measured by cytometric bead array (CBA, BD Biosciences, USA) according to the manufacturer's instructions. A flow cytometer was used for these analyses (FACSCalibur, BD Biosciences, USA). The data were analysed using FCAP Array 1.0 software (CBA, BD Biosciences, USA).

### **Physical growth and motor performance evaluation**

Body mass: Total body mass was determined following the recommendations of Gordon

*et al.* (1991) for children from 5 to 10 years old and from 10 to 15 years old using a digital scale with a range of 0 to 150 kg and a precision of 200 g.

**Height:** The height of the individuals in the orthostatic position was determined following the procedures of Gordan *et al.* (1991) for children from 5 to 10 years old and from 10 to 15 years old using a wooden stadiometer graduated in millimetres with a range of 0 to 2.50 m.

### Motor performance evaluation

**Flexibility test:** To measure the muscular power of the upper limbs, the flexibility of the dorso-lumbar region was evaluated using a modified wooden box with dimensions of 30.5 x 30.5 x 30.5 cm and a surface of 70 cm following the modified procedure recommended by Hoeger *et al.* (1992).

**Abdominal test:** The strength of the abdominal muscles was evaluated on a mattress with hands at the nape of the neck and the knees semi-flexed (both sexes) for one minute using a precision Casio chronometer (1/100 sec.) following the recommendations of de Soares *et al.* (1983).

**Standing distance jump test:** The muscular power of the lower limbs was evaluated on a soft flat surface; the distance jumped was measured following the recommendations proposed by Soares *et al.* (1983) with a tape measure with an accuracy of 0.1 cm and a range of 0 to 3 m.

**Speed test:** To evaluate the aerobic capacity, the time to run a distance of 20 m was evaluated. A precision Casio chronometer (1/100 sec) was used; the timer was started the moment the individual took the first step from the start line and was stopped at the moment the individual passed the finish line.

### Statistical analysis

The means and their respective standard deviations (SDs) of hormone levels, cytokine concentrations and physical performance were calculated for the groups of parasitized and unparasitized school children, and Student's t-test was used to verify differences in the means between those groups. Correlations among cytokines, hormones

and physical performance were evaluated using Pearson's linear correlation test. Statistical significance was considered for a p-value lower than 0.05 ( $p < 0.05$ ).

## RESULTS

The prevalence of parasitic infection among the students studied was 7,98%. Among the 25 parasitized students, *Schistosoma mansoni* was the most prevalent parasite (80%), while the others were infected (20%) by *Enterobius vermicularis*, *Ancylostomatidae* spp., or *Ascaris lumbricoides*. Table 1 presents the general characteristics and anthropometric data of the students. Other than the presence of parasites, there were no differences between the groups.

Table 2 shows the serum cytokine levels in the students. IL-12 and TNF- $\alpha$  levels were higher in serum from students positive for

Table 1. Anthropometric data of school children with parasitic infection

Parameters	Parasitic Infection	
	Negative	Positive
Age (years)	9.8 $\pm$ 1.1	9.9 $\pm$ 0.8
Body Mass (kg)	36.5 $\pm$ 8.6	36.3 $\pm$ 7.1
Stature (cm)	141 $\pm$ 10	143 $\pm$ 10
BMI	17.7 $\pm$ 2.2	17.4 $\pm$ 2.4
Eutrophic	76%	70%
Overweight	20%	20%
Obese	4%	10%

BMI = body mass index.

Table 2. Cytokine concentrations (pg/mL) in the serum of students with parasitic infection

Cytokines	Parasitic Infection	
	Negative	Positive
IL-1 $\beta$	7.5 $\pm$ 3.1	9.1 $\pm$ 2.9
IL-6	4.2 $\pm$ 2.0	3.9 $\pm$ 1.3
IL-8	115.0 $\pm$ 83.3	26.7 $\pm$ 15.5*
IL-10	5.6 $\pm$ 1.1	5.9 $\pm$ 1.3
IL-12	7.6 $\pm$ 4.4	45.7 $\pm$ 21.2*
IL-17	22.5 $\pm$ 6.9	31.0 $\pm$ 12.1
TNF- $\alpha$	5.1 $\pm$ 1.9	20.5 $\pm$ 8.6*

The results represent the mean and SD of 25 different individuals. \*indicates intergroup differences ( $p < 0.05$ ).

parasitic infection than in that from parasite-negative students, whereas IL-8 levels were lower in parasite-positive students than in parasite-negative students. The IL-1 $\beta$ , IL-6, IL-10 and IL-17 levels were similar between the groups.

Serum from students who were positive for parasitic infection showed higher levels of melatonin than that of the students negative for parasitic infection. The cortisol levels were similar between the groups studied (Figure 1).

There was no difference in aerobic capacity between school children with parasitic infection and non-parasitized school children. School children positive for parasitic infection presented higher strength of the lower limbs than did the unparasitized children, while the strength of the upper limbs of the school children was similar between the groups. There was a reduction in abdominal performance in school children with parasitic infection.

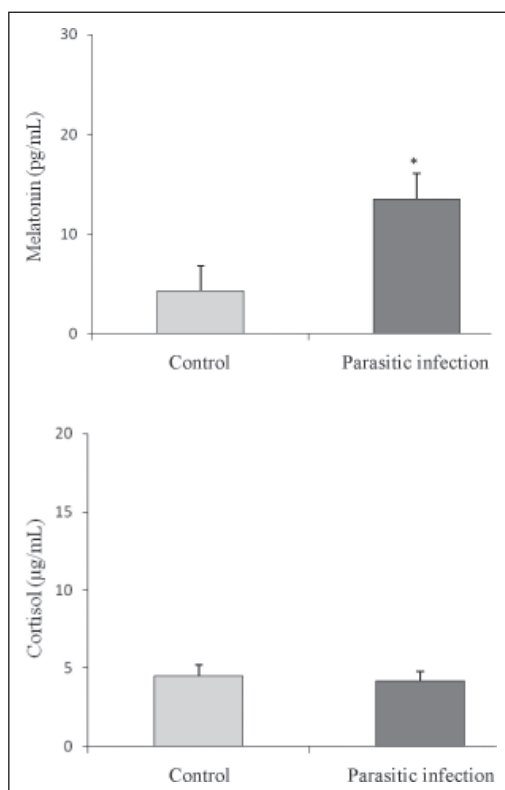


Figure 1. Melatonin (pg/mL) and cortisol (pg/mL) levels in serum from school children. \* Statistical difference between the groups ( $P < 0.05$ ).

Correlations among cytokine and hormone levels and physical performance were evaluated with Pearson's test. The control group exhibited a negative correlation between melatonin levels and the levels of IL-1 $\beta$  and IL-6, whereas cortisol showed a negative correlation with IL-17. In the parasitic infection group, IL-12 levels were positively correlated with melatonin levels (Table 3).

Regardless of the presence of parasitic infection, none of the physical performance parameters evaluated correlated with the serum levels of hormones (melatonin and cortisol) in the school children (Table 4).

Analysis of correlations between physical performance and cytokine/chemokine levels showed that in the control group, there was a positive correlation between IL-1 and upper-limb strength. The chemokine IL-8 showed a positive correlation with abdominal performance, and IL-12 presented a negative correlation with lower-limb strength (Table 5). In the parasitic infection group, the chemokine IL-8 showed a positive correlation with aerobic capacity, while IL-17 and TNF- $\alpha$  showed a positive correlation with abdominal performance. However, with respect to IL-6 and IL-10 levels, no correlations ( $p > 0.05$ ) were found with physical performance (Table 5).

## DISCUSSION

Parasitic infections, especially in developing countries, constitute a serious public health problem (Ostan *et al.*, 2007; Basso *et al.*, 2008), and children are more vulnerable to intestinal parasites than are other age groups (Montresor *et al.*, 2002). This study describes the serum cytokine and hormone concentrations and the physical performance of children infected with enteroparasites and examine the correlation between these variables.

The prevalence of parasitic infection depends on external environmental factors and factors inherent to individuals (Frei *et al.*, 2008). In this study, the majority of school children were residents of rural areas and despite the supply of treated water and

Table 3. Correlations between cytokines/chemokines and the hormones melatonin and cortisol in serum from school children

Cytokines/ Chemokines	Melatonin		Cortisol	
	Control	Parasitic infection	Control	Parasitic infection
IL-1 $\beta$	<b>r= -0.6272;</b> <b>P=0.0092</b>	r= -0.2150; P=0.4072	r= -0.2753; P=0.3020	r= -0.1004; P=0.7115
IL-6	<b>r= -0.5340;</b> <b>P=0.0331</b>	r= 0.0795; P=0.7617	r= 0.1734; P=0.5207	r= 0.0682; P=0.8018
IL-8	r= -0.0579; P=0.8314	r= 0.2167; P=0.4034	r= -0.3380; P=0.2003	r= -0.4190; P=0.8776
IL-10	r= -0.1367; P=0.6138	r= 0.0823; P=0.7534	r= 0.1736; P=0.5202	r= -0.3712; P=0.1569
IL-12	r= -0.2888; P=0.2779	<b>r= 0.6254;</b> <b>P=0.0303</b>	r= -0.0953; P=0.7255	r= -0.2238; P=0.4048
IL-17	r= -0.2080; P=0.4395	r= 0.2761; P=0.3850	<b>r= -0.5742;</b> <b>P=0.0199</b>	r= -0.3854; P=0.2159
TNF- $\alpha$	r= -0.3529; P=0.1799	r= -0.0778; P=0.7668	r= 0.1946; P=0.4703	r= 0.3766; P=0.1505

Table 4. Correlations between physical performance and the hormones melatonin and cortisol in serum from school children

Physical Performance	Melatonin		Cortisol	
	Control	Parasitic infection	Control	Parasitic infection
Aerobic capacity	r= 0.3619; P=0.1683	r= 0.0427; P=0.8708	r= -0.2216; P=0.4094	r= 0.2186; P=0.4159
Lower-limb strength	r= 0.3164; P=0.2324	r= 0.1752; P=0.5013	r= 0.0961; P=0.7232	r= -0.0247; P=0.9276
Upper-limb strength	r= -0.0538; P=0.8431	r= 0.4060; P=0.1058	r= -0.1825; P=0.4986	r= 0.0351; P=0.8974
Abdominal performance	r= 0.2826; P=0.2888	r= -0.1496; P=0.5666	r= -0.2143; P=0.4255	r= 0.3286; P=0.2140

regular garbage collection, most still use a sewer for domestic sewage and bury or burn domestic waste, which may contribute to the persistence and prevalence of parasites in this community, that was 7.98%. Among the infected students, 80% were infected by *S. mansoni* and 20% were infected by *E. vermicularis*, *Ancylostomatidae* spp., or *A. Lumbricoides*.

In parasitic infections, several effectors mechanisms of the immune system are activated that are capable of controlling

infection (Moraes *et al.*, 2015); these mechanisms generate inflammation that can be regulated by several biochemical signals, with cytokines being one of the most important mediators of this condition (Morais *et al.*, 2015; Fagundes *et al.*, 2016; Fujimori *et al.*, 2017; Fagundes *et al.*, 2018).

The immune response to helminth infection, such as *S. mansoni* infection, is a complex immune process, especially in the acute phase that depends on the intensity and severity of the disease (Araujo *et al.*, 2004).



Table 5. Correlations between cytokines/chemokines and the physical performance of school children

Cytokines/ Chemokines	Groups	Aerobic Capacity	Lower-Limb Strength	Upper-Limb Strength	Abdominal Performance
IL-1 $\beta$	Control	r= -0.3820; P=0.072	r= -0.1820; P=0.3878	<b>r= 0.6032;</b> <b>P=0.0103</b>	r= -0.0106; P=0.9618
	Parasitic infection	r= -0.3565; P=0.1601	r= -0.1169; P=0.6549	r= 0.0727; P=0.7817	r= -0.0386; P=0.8832
IL-6	Control	r= -0.1869; P=0.3931	r= -0.2117; P=0.3322	r= -0.3330; P=0.1204	r= 0.2885; P=0.1818
	Parasitic infection	r= 0.1340; P=0.6207	r= -0.0356; P=0.8959	r= 0.2505; P=0.3493	r= -0.1632; P=0.5459
IL-8	Control	r= 0.1402; P=0.5234	r= -0.1097; P=0.6182	r= -0.2369; P=0.2765	<b>r=0.4439;</b> <b>P=0.0338</b>
	Parasitic infection	<b>r= 0.5906;</b> <b>P=0.0455</b>	r= -0.3190; P=0.2120	r= -0.0676; P=0.7965	r= 0.0515; P=0.8744
IL-10	Control	r= 0.1366; P=0.5343	r= 0.0825; P=0.7084	r= -0.1254; P=0.5685	r=0.1399; P=0.5244
	Parasitic infection	r= -0.2854; P=0.2668	r= 0.3830; P=0.1291	r= 0.1149; P=0.6604	r= -0.2113; P=0.4156
IL-12	Control	r= -0.2524; P=0.2452	<b>r= -0.4670;</b> <b>P=0.0246</b>	r= -0.3543; P=0.0971	r= -0.1555; P=0.4787
	Parasitic infection	r= -0.0164; P=0.8149	r= 0.0455; P=0.8625	r= -0.2787; P=0.2786	r= 0.0152; P=0.9538
IL-17	Control	r= 0.0911; P=0.6867	r= -0.1856; P=0.4083	r= 0.1000; P=0.9100	r=0.3335; P=0.1293
	Parasitic infection	r= -0.1030; P=0.7502	r= -0.2544; P=0.4248	r= -0.1129; P=0.7269	<b>r= 0.6014;</b> <b>P=0.0385</b>
TNF- $\alpha$	Control	r= -0.3727; P=0.0798	r= 0.0252; P=0.9091	r= -0.0122; P=0.9560	r= -0.1943; P=0.3743
	Parasitic infection	r= -0.1655; P=0.5256	r= -0.1730; P=0.5067	r= -0.2139; P=0.4097	<b>r= 0.4309;</b> <b>P=0.0481</b>

In the acute phase of infection, there is an elevation in the cellular response, whereas in the chronic phase, there is a reduction of this immune response. In this study, we observed a proinflammatory response (Th1) with increased IL-12 and TNF- $\alpha$  in the serum of students with parasitic infection. These cytokines are involved in the eradication of various infectious diseases (Vernal *et al.*, 2008; Heo *et al.*, 2010).

Studies have reported that TNF- $\alpha$  can modulate helminth infections by regulating the expression of IL-4 and IL-13 receptors in the cells of the intestinal microenvironment (Lugli *et al.*, 1997), and it is believed that this cytokine regulates the responses of Th2 cytokines in the intestine and exerts a

significant effect on the protective immunity to parasitic infection due to complex interactions in the cytokine network (Artis *et al.*, 1999).

In this study, parasitic infection reduced IL-8 in the serum of school children. IL-8 is a chemokine that is related to a variety of diseases. It has the ability to promote the migration of cells such as neutrophils, monocytes and T cells and increases inflammation (Pepper, 1997). This chemokine is capable of reducing the production of IgE stimulated by IL-4 (Baggiolini *et al.*, 1994). Considering that IgE is an important part of the immune mechanism for the elimination of helminths, the reduction of IL-8 in the serum of parasitized school children suggests an

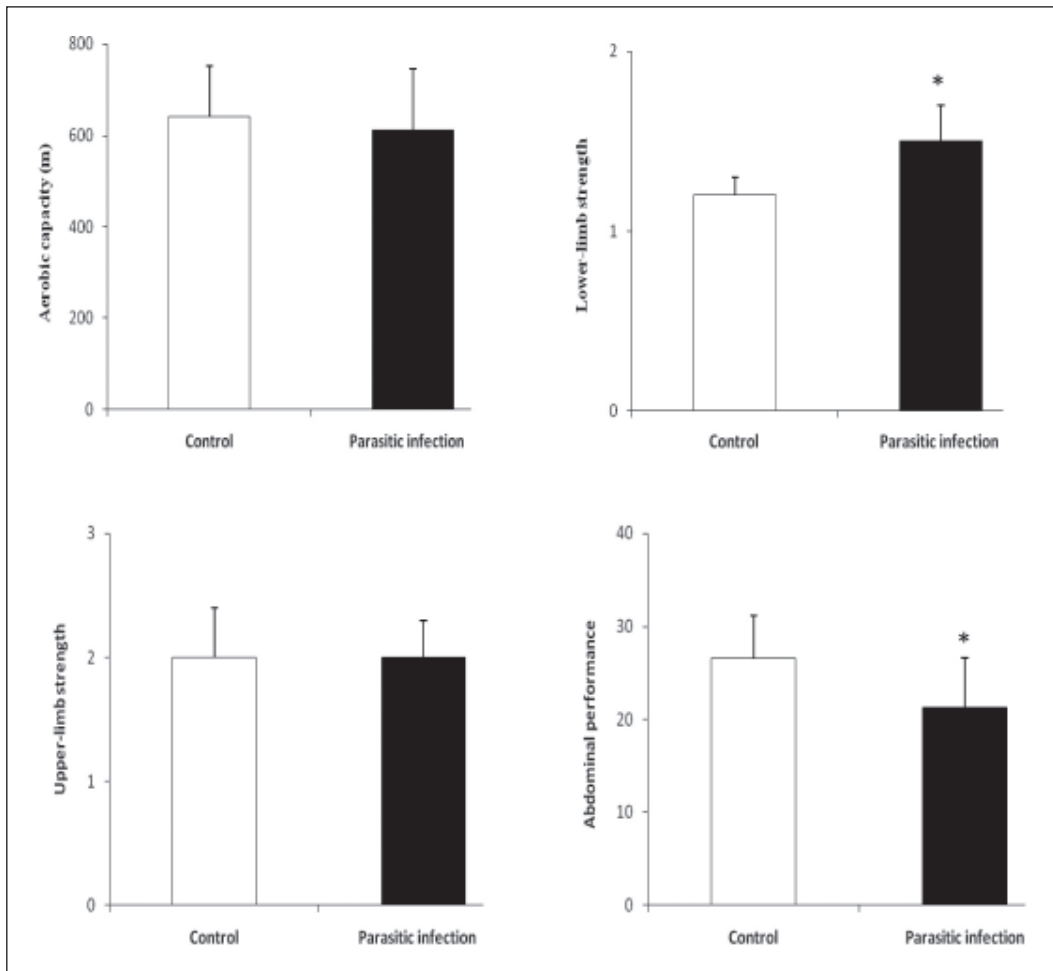


Figure 2. Aerobic capacity (A), lower-limb strength (B), upper-limb strength (C) and abdominal performance (D) of school children with positive parasitological examinations. The results represent the mean and the standard error.  $P < 0.05$ .

immunological control mechanism targeting an increase in IgE-mediated responses and favouring the elimination of the parasites.

Interactions among cytokines and hormones have been reported in several studies. Elevated levels of melatonin in the blood have been associated with increased IL-12 (García-Mauriño, 1999). In this work, in addition to the increased IL-12 and TNF- $\alpha$ , high concentrations of the hormone melatonin were found in the serum of parasitized school children.

Melatonin exerts several functions in the body and has been extensively studied (Maestroni, 2001; Srinivasan *et al.*, 2008; França-Botelho *et al.*, 2011; Hara *et al.*, 2013; Honorio-França *et al.*, 2013). The beneficial

actions of melatonin are associated with its ability to remove free radicals and increase the activity of antioxidant enzymes (Sudnikovich *et al.*, 2007; Pandi-Perumal *et al.*, 2008). In addition, melatonin has immunomodulatory effects (Besedovsky *et al.*, 1996; Honorio-França *et al.*, 2013; Hara *et al.*, 2013; Pereira *et al.*, 2018) and reduces the severity of *E. histolytica* (França-Botelho *et al.*, 2011) and *T. cruzi* (Santelo *et al.*, 2007) infections, suggesting effective therapeutic action in the treatment of these protozoa.

Due to the anti-inflammatory properties of melatonin (Reiter *et al.*, 1995; Morceli *et al.*, 2013), the increase in this hormone in the serum of parasitized school children may



reduce the inflammatory effects of the cytokines IL-12 and TNF- $\alpha$ , which explains the modulation of the immune response and tissue protection during infection (Carrillo-Vico *et al.*, 2004; Fernandes *et al.*, 2006), in addition to inhibiting the hormone cortisol (Gunn *et al.*, 2016). Cortisol is an important hormone in the inflammatory process (Fagundes *et al.*, 2012) and immune response (Bonga, 1997; Fagundes *et al.*, 2012).

Children of low socioeconomic status are part of a vulnerable group of risk due to the stressful experience early in life, which can cause a cortisol dysregulation. In this study, the presence of parasites did not alter the levels of this hormone, which reinforces the hypothesis that the increase in melatonin reduces cortisol levels.

Interestingly, the hormone cortisol had a negative correlation with IL-17. There is a close relationship between hormones, cytokines and neuropeptides that modulate the host immune response, including both cellular and humoral immunity (Aguilar-Díaz *et al.*, 2015). During many parasitic infections, there is a reciprocal relationship amongst hormones, the immune system, and the eventual elimination or establishment of the parasites in humans (Hernández-Bello *et al.*, 2010). Both cortisol (Fagundes *et al.*, 2012) and IL-17 (Papu *et al.*, 2012) appear to be involved in inflammatory processes. In malaria, IL-17 plays an important role (Scherer *et al.*, 2016), but further studies should be conducted to investigate the effects of the interaction of this cytokine and cortisol.

Additionally, in this work, a positive correlation between melatonin and IL-12 was observed in students with parasitic infection, suggesting that in the presence of infection, melatonin interacts with mediators of inflammation. In the literature, other studies have also reported that melatonin may modulate mediators of inflammation (García-Mauriño *et al.*, 1999; Carrillo-Vico *et al.*, 2004; Fernandes *et al.*, 2006).

Inflammation is a physiological response of the immune system to infectious agents or tissue damage. A previous study reported that physical exercise may have anti- or

proinflammatory effects and may protect or expose the body to the development of various chronic and infectious diseases (Warren *et al.*, 2010).

The responses promoted by exercise, both acute and chronic, change various immunological parameters. Moderate exercise may stimulate cellular immunity and thereby decrease the risk of infection, while high-intensity exercise may promote a decrease in the immune system and increase the risk of infectious diseases (Pedersen *et al.*, 2000).

In this study, the physical performance of students, regardless of the presence of parasites, was similar with regard to aerobic capacity and upper-limb strength. However, students with parasitic infections, despite having greater muscle strength of the lower limbs, had a reduction in abdominal performance. As these students were mostly infected with helminths, this reduction in abdominal performance may be a direct effect of parasitic infection.

It should also be considered that despite the presence of parasites, these children presented normal physical growth data, which may have contributed to maintaining reasonable physical performance, since studies suggest that well-nourished children with nutrient reserves are less susceptible to the harmful effects of parasites (Lazarte *et al.*, 2015).

Serum levels of cytokines can be modulated by various stimuli, including hormones, oxidative stress, and exercise (Cannon, 2000). Several studies have reported increased serum cytokine levels after different forms of exercise (Terra *et al.*, 2012). In this study, cytokines and physical performance were correlated. It was observed in the parasitized group that there was a positive correlation between IL-8 and aerobic capacity and between IL-17/TNF $\alpha$  and abdominal performance.

IL-8 promotes increased oxidative metabolism (Zwahlen *et al.*, 1993) and is normally stimulated by TNF $\alpha$  (Baggiolini *et al.*, 1994) and by IL-17 (Fossiez, 1996). TNF $\alpha$  also promotes increases in oxidative metabolism and helps in the production of

proteins (Mackay *et al.*, 1993; Tartaglia *et al.*, 1993), and in individuals with high physical performance, there is a decrease in this cytokine (Bruunsgaard, 2005).

Therefore, according to the data of this study, it can be suggested that parasitic infection influenced abdominal performance, since the parasitized group presented lower abdominal performance and a correlation between abdominal performance and IL-17 and TNF $\alpha$ . Studies have reported that one of the clinical features of *S. mansoni* infestation is abdominal muscle pain (Huggins *et al.*, 1998). Therefore, it is likely that the concentration of TNF $\alpha$  is elevated, inducing an acute inflammatory process in the combat against parasitic infection (Willerson *et al.*, 2004). However, further studies are needed to better understand the effects on physical capacity in children with parasites.

Interaction between exercise and hormones has also been reported, and studies suggest that melatonin may have a favourable influence on many systems in the body (Escames *et al.*, 2010). Melatonin, as well as the immune system, acts as a regulatory factor and appears to inhibit inflammation in an intensity-dependent manner during exercise. Melatonin levels increase after exercise in a transient and short-term process, but a decrease or no change in the amount of melatonin has also been reported after exercise (Beck *et al.*, 2016; Zarei *et al.*, 2016). In this study, both melatonin and cortisol were correlated with physical exercise, but the correlation was independent of the presence of parasites.

In conclusion, these data suggest that parasitic infections determine a profile of inflammatory cytokines and that melatonin, due to its anti-inflammatory properties, could be involved in the control of this process to minimize tissue damage. The difficulty of the students in practising physical exercises, especially those regarding abdominal performance should be considered, since this difficulty can be an indication of enteroparasitic infection. Therefore, physical educators should be informed so that they can observe these difficulties and

guide students to undergo parasitological examinations.

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