Journal of Helminthology (2017) **91**, 278–283
doi:10.1017/S0022149X16000286

The relationship between helminth infections and low haemoglobin levels in Ethiopian children with blood type A

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(Received 16 January 2016; Accepted 22 April 2016; First published online 19 May 2016)

Abstract

The current study was conducted to evaluate the nature of association of ABO blood type with helminth infection and related reduction in haemoglobin concentration. Stool samples were collected from 403 school-age children attending Tikur Wuha Elementary School from February to April 2011. Helminth infection was examined using formol-ether concentration and thick Kato–Katz (two slides per stool specimen) techniques. Haemoglobin level was determined using a HemoCue machine and ABO blood type was determined using the antisera haemagglutination test. Nutritional status was assessed using height and weight measurements. Out of 403 children examined, 169, 120, 96 and 18 had blood type O, A, B and AB, respectively. The prevalences of helminth infections were 46.9% for hookworm, 24.6% for *Schistosoma mansoni*, 4.2% for *Ascaris lumbricoides*, 1.7% for *Trichuris trichiura* and 58.3% for any helminth species. The relative odds of infection with at least one helminth species was significantly higher among children with blood type A (adjusted odds ratio (AOR), 2.10; 95% confidence interval (CI), 1.28–3.45) or blood type B (AOR, 2.08; 95% CI, 1.22–3.56) as compared to children with blood type O. Among children infected with helminths, mean haemoglobin concentration was lower in those with blood type A than those with blood type O (β, −0.36; 95% CI, −0.72 to −0.01). The relative odds of hookworm infection (AOR, 1.78; 95% CI, 1.08–2.92) and related reduction in haemogobin levels (β, −0.45; 95% CI, −0.84 to −0.04) was higher among children with blood type A as compared to those with blood type O. Although the difference was not significant, the relative odds of *S. mansoni* or *A. lumbricoides* infections and related reduction in haemoglobin levels was also higher in children with blood type A or B as compared to children with blood type O. In conclusion, children with blood type A are associated with an increased risk of helminth, particularly hookworm, infection and related reduction in haemoglobin level. The mechanisms by which blood type A makes children susceptible to helminth infection and a related reduction in haemoglobin level ought to be investigated.

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Introduction

Soil-transmitted helminths (STHs) and *Schistosoma mansoni* infections are common public health problems of school-age children living in sub-Saharan Africa (Hotez *et al*., 2008; Pullan & Brooker, 2008). Different environmental and social factors affect the chance of contact between humans and infective stages of helminths (Hotez *et al*., 2008). However, the successful entry, survival and multiplication of the infective stages of helminths in humans is largely dependent on the genetic and immune status of the host (Quinnell, 2003).

The ABO blood type is hypothesized to be one among other genetic factors that affect susceptibility or resistance of individuals to helminth infections (Berger *et al*., 1989). However, the epidemiological evidence to support this notion is varied. Some studies documented increased risk of *S. mansoni* infection and related clinical outcomes in individuals with blood type A (Ndamba *et al*., 1997; Degarege *et al*., 2015), while other studies reported a lack of association between ABO blood type and prevalence or intensity of helminth infection and related morbidity (Gabr & Mandour, 1991; Cooper *et al*., 1993; Degarege *et al*., 2014). Hence, the current study was conducted to evaluate the nature of association of ABO blood type with helminth infection and related reduction in haemoglobin level among school-age children attending Tikur Wuha Elementary School, in north-western Ethiopia.

Methods

Study area and population

Between February and March 2011, 403 school-age children attending Tikur Wuha Elementary School in north-western Ethiopia were recruited to participate in a cross-sectional study. The school is situated in Jiga District, which is located 390 km north of Addis Ababa, Ethiopia. The area has a longitude and latitude of 10°42′ N 37°20′E and lies at an altitude of 1917 m above sea level. The district has an average annual temperature of 18.5°C and mean annual rainfall of 134.35 mm. All volunteer children aged between 5 and 15 years were included in the study. The study participants apparently looked healthy and were without fever. However, individuals aged above 15 years and those with fever were excluded from the study. The study participants were from the same area and had similar housing conditions, life style, ethnicity and socio-economic status of their families.

Nutritional status and measurements of haemoglobin/blood type

Nutritional status was measured based on height (measured to the nearest 100 cm) and weight (measured to the nearest 1 kg). Then, *z* values for weight-for-age, body mass index-for-age and height-for-age were calculated, based on which the nutritional status of children was determined (World Health Organization, 2009, 2010).

About 10 µl of finger-prick blood was collected from each child and used to assess haemoglobin level and blood type. Haemoglobin level was determined using a HemoCue machine (HemoCue Hb201, Anghelom, Sweden), based on which the anaemic status of the children was determined (World Health Organization, 2001). Blood type was determined using commercial antisera A, antisera B and antisera D (Tulip Diagnostics (p) Ltd, Verna, India).

Helminth infections

Approximately 5 g of fresh stool were collected from volunteer children between 10.00 a.m. and 4.00 p.m. The stool sample was processed using Kato–Katz (two slides per individual) and concentration techniques (World Health Organization, 1991). Qualitative examination for helminth infection and egg counting in the case of hookworm infection from the Kato–Katz slides were performed on the spot. However, egg counts for other helminth species from the Kato–Katz slides and qualitative examination using formal-ether concentration were conducted after transporting the samples to the laboratory at Aklilu Lemma Institute of Pathobiology (ALIPB), Addis Ababa University.

Data analysis

Data were analysed using STATA version 11 (Stata Corporation, College Station, Texas, USA). Chi-square analysis was used to test the association of prevalence of helminth infection with ABO blood type. As the distribution of eggs of different helminth species was not normal, a Kruskal–Wallis rank test was used to test whether the differences in mean egg counts of helminths across blood types were significant. In order to test the hypothesis that the ABO blood type affects the odds of helminth infection and related anaemia, a multiple logistic regression analysis adjusted for the effects of age, sex, nutritional status and multiple infections with different helminth species was used. To test the hypothesis that ABO blood type impacts the intensity of helminth infection and related reduction in haemoglobin level, a multiple linear regression analysis that controlled for age, sex, nutritional status and multiple infections with different helminth species was used. The logarithms of eggs/g of hookworm, *S. mansoni*, *Ascaris lumbricoides* and *Trichuris trichiura* were calculated before being fitted in the regression models. CI values (95% confidence intervals) were calculated for the odds ratio (OR) and regression coefficient estimates (β). Values were considered significant whenever the *P* value was less than 5%.

Ethical consideration

Permission to conduct the study was obtained from the school directors. Children participated in the study after their parents or guardians provided oral consent. Assent was also sought from children who participated in the study. Children who were found to be infected with STHs were treated with 400 mg albendazole, while those who were found to be infected with *Hymenolepis nana*, *Taenia saginata* and *S. mansoni* were treated with praziquantel in appropriate doses.

https://doi.org/10.1017/S0022149X16000286 Published online by Cambridge University Press

Table 1. The prevalence (%) of infection and mean number of eggs/g faeces (EPG) of helminth parasites in children from Ethiopia, relative to blood types; *N* = number of children examined.

		Hookworm		*S. mansoni*		*A. lumbricoides*		*T. trichiura*		Any
Blood types	*N*	%	EPG	%	EPG	%	EPG	%	EPG	helminth %
A	120	53.3	179.2	27.5	55.3	5.8	562.3	1.7	180.0	66.7
B	96	55.2	215.1	27.1	71.1	4.2	714.0	1.0	3912.0	67.4
AB	18	36.8	161.1	31.6	96.0	10.5	1200.0	0.0	0.0	47.4
O	169	38.5	187.6	20.1	86.1	2.4	2826.0	2.4	42.0	48.5
Total	403	46.9	191.5	24.6	72.5	4.2	1205.6	1.7	634.3	58.3
P value		0.014	0.509	0.352	0.881	0.253	0.531	0.803	0.273	0.003

Table 2. The effect of ABO blood types on helminth infections in children from Ethiopia, based on crude and adjusted odds ratios (OR) for age, gender, nutritional status and multiple infections; CI, 95% confidence intervals.

Helminths	Blood types	Crude OR	CI	Adjusted OR	CI
Hookworm	A	1.83	1.14–2.94	1.78	1.08–2.92
	B	1.97	1.19–3.28	1.77	1.04–3.00
	AB	1.02	0.38–2.76	0.78	0.28–2.18
S. mansoni	A	1.51	0.87–2.61	1.27	0.70–2.29
	B	1.47	0.82–2.65	1.46	0.79–2.72
	AB	1.99	0.69–5.67	1.74	0.58–5.21
A. lumbricoides	A	2.55	0.73–8.93	2.38	0.60–9.35
	B	1.79	0.44–7.34	1.78	0.40–7.98
	AB	5.16	0.88–30.37	5.38	0.81–35.70
T. trichiura	A	0.69	0.13–3.88	0.37	0.05–2.58
	B	0.43	0.05–3.94	0.21	0.02–2.39
	AB	–	–	–	–
Any helminth	A	2.12	1.31–3.44	2.10	1.28–3.45
	B	2.12	1.26–3.57	2.08	1.22–3.56
	AB	1.06	0.40–2.80	0.85	0.32–2.26

Results

ABO blood types and helminth infections

Of the 403 schoolchildren, 53.9% were female (mean age in years ± standard deviation: 11.42 ± 2.42). There were 169 (41.9%) children with blood type O, 120 (29.8%) with type A, 96 (23.8%) with type B and 18 (4.5%) with type AB. About 58.3% of the children were infected with at least one helminth species: hookworm (46.9%), *S. mansoni* (24.6%), *A. lumbricoides* (4.2%) and *T. trichiura* (1.7%) infections (table 1).

The prevalence of helminth infection was higher in children with blood type A or B than those with blood type O ($P = 0.003$). Particularly, hookworm infection was more common in children with blood type A and B than those with blood type O ($P = 0.014$). However, the difference in the prevalence of *S. mansoni* and *A. lumbricoides* infection was not significant across the different blood types.

The chance of hookworm infection was significantly higher among children with blood type A (adjusted odds ratio (AOR), 1.78; 95% CI, 1.08–2.92) or blood type B (AOR, 1.77; 95% CI, 1.04–3.00) as compared to blood type O. Although the difference was not significant, the odds of *S. mansoni* and *A. lumbricoides* infections were also higher in children with blood type A, B or AB as compared to children with blood type O (table 2). Overall, the relative odds of infection with at least one helminth species was significantly higher among children with blood type A (AOR, 2.10; 95% CI, 1.28–3.45) or blood type B (AOR, 2.08; 95% CI, 1.22–3.56) as compared to children with blood type O.

The mean number of eggs/g of hookworm, *S. mansoni*, *A. lumbricoides* and *T. trichiura* infections were 191.49 (range 24–1272), 72.48 (range 24–432), 1205.64 (range 24–8664) and 634.28 (range 24–3912), respectively. Hookworm egg intensity was similar when comparing children with blood type O and those with blood type A, B or AB (table 3). The differences in egg intensity of *S. mansoni*, *A. lumbricoides* and *T. trichiura* were also similar when comparing children with blood type O and those with blood type A, B or AB (table 3).

ABO blood types and haemoglobin level

Children with blood types A, B, AB and O, and a helminth infection, had haemoglobin levels of 12.57, 12.69, 12.31 and 12.92 g/dl, respectively. Among children infected with at least one species of helminth, the mean haemoglobin concentration was lower in those with blood type A compared to those with blood type O (β, −0.36; 95% CI, −0.72 to −0.01). Similarly, among children infected with hookworm, the mean haemoglobin concentration was lower in those with blood type A

https://doi.org/10.1017/S0022149X16000286 Published online by Cambridge University Press

Table 3. The effect of ABO blood types on mean egg/g (EPG) of helminths in children from Ethiopia, based on unadjusted and adjusted regression coefficients (β) for age, sex, nutritional status and multiple helminth infection; CI, 95% confidence intervals.

Helminths	Blood types	Unadjusted β	CI	Adjusted β	CI
Hookworm	A	−0.06	–0.37–0.25	–0.06	–0.37–0.26
	B	0.16	–0.17–0.48	0.16	–0.17–0.49
	AB	–0.04	–0.74–0.65	–0.03	–0.74–0.68
S. mansoni	A	–0.17	–0.54–0.20	–0.11	–0.50–0.28
	B	–0.05	–0.44–0.35	–0.04	–0.44–0.37
	AB	0.18	–0.49–0.86	0.21	–0.48–0.91
A. lumbricoides	A	–1.37	–3.62–0.88	–2.08	–5.96–1.79
	B	–1.61	–4.16–0.92	–3.10	–8.00–1.80
	AB	–1.76	–4.88–1.34	–2.85	–8.12–2.42
T. trichiura	A	0.87	–1.64–3.38	1.88	–5.72–9.48
	B	4.64	1.40–7.89	4.40	–1.35–10.14
	AB	–	–	–	–

Table 4. The effect of ABO blood type on helminth infection relative to haemoglobin concentration and prevalence of anaemia in children from Ethiopia, based on regression coefficients (β) and odds ratio (OR) adjusted for age, sex, nutritional status and multiple helminth infection; CI, 95% confidence intervals.

Helminths	Blood types	Adjusted β	CI	Adjusted OR	CI
Hookworm	A	−0.45	−0.84 to –0.04	2.36	0.86–6.50
	B	−0.24	−0.66–0.17	1.89	0.68–5.26
	AB	−0.36	−1.26–0.54	0.83	0.07–9.26
S. mansoni	A	−0.49	−1.09–0.11	2.02	0.54–7.59
	B	−0.21	−0.83–0.41	2.15	0.54–8.47
	AB	−0.19	−1.25–0.86	0.62	0.05–8.12
A. lumbricoides	A	−0.05	−1.05–0.96	–	–
	B	−1.10	−2.41–0.20	–	–
	AB	−1.31	−2.88–0.26	–	–
T. trichiura	A	−3.51	−12.08–5.06	–	–
	B	−3.34	−9.82–3.14	–	–
	AB	–	–	–	–
Any helminth	A	−0.36	−0.72 to –0.01	1.82	0.77–4.33
	B	−0.18	−0.56–0.19	1.94	0.79–4.71
	AB	−0.53	−1.32–0.27	0.62	0.28–9.38

compared to those with blood type O (β, −0.45; 95% CI, −0.84 to −0.04). However, mean haemoglobin concentration among children infected with *S. mansoni*, *A. lumbricoides* or *T. trichiura* was similar among all blood types (table 4). The odds of anaemia in children infected with *S. mansoni*, *A. lumbricoides* or *T. trichiura* were also similar among all blood types (table 4).

Discussion

The present study indicated that children with blood type A are associated with increased odds of helminth infection and a related reduction in mean haemoglobin level. The findings suggest that the ABO blood type might be linked with helminth infection and related clinical outcomes. In light of this, children with blood type A may be more susceptible to helminth, particularly hookworm, infection and related reduction in haemoglobin level, while children with blood type O could be partially protected against the infection and related anaemia.

Different helminth species such as hookworms, *S. mansoni* and *A. lumbricoides* contain polysaccharides that may resemble molecularly the substances in blood type A (Oliver-gonzalez & Gonzalez, 1949; Ottsen, 1985; Haseeb *et al.*, 2008). As a result, it is hypothesized that these parasites may not be considered as foreign and could escape the host immune response during infection in individuals with blood type A (Berger *et al.*, 1989). Indeed, anti-A antibodies failed to recognize *A. lumbricoides* antigens isolated from individuals with blood type A (Deleon *et al.*, 2000; Deleon & Valverdeh, 2003). This supports the notion that *A. lumbricoides* may have molecules that resemble the antigen of blood type A, or that the parasite may adsorb blood type A antigens. In addition, the increased odds of helminth infection among children with blood type A might be due to the possibility that blood type A antigens could contain an increased amount of glycolipid substances that serve as adhesion receptors for hookworm, *S. mansoni* and *A. lumbricoides* antigens (Berger *et al.*, 1989). This will help the parasites to survive and multiply easily within the host, causing severe intestinal damage and high blood loss.

https://doi.org/10.1017/S0022149X16000286 Published online by Cambridge University Press

Previous studies have also documented high prevalence or intensity of *S. mansoni* infection in children with blood type A (Ndamba *et al.*, 1997; Degarege *et al.*, 2015). The number of children infected with *A. lumbricoides* ($n = 17$) or *S. mansoni* ($n = 99$) in the present study was small. This could be the reason why the difference in the prevalence of infection with *A. lumbricoides* or *S. mansoni* was not significant when compared across the different blood types in the current study.

The reduction in mean haemoglobin level due to helminth infection was also significantly higher in children of blood type A than in those of blood type O. Another study in Ethiopia also documented a significantly lower mean haemoglobin level among patients with blood type AB and slightly lower haemoglobin level in those with blood types A and B than in patients with blood type O (Degarege *et al.*, 2014). This could be due to the increased occurrence of helminths in children with blood type A, which may differentially cause high blood loss and malabsorption. Another hypothesis is that, due to relatedness between blood type A and helminth antigens (Oliver-gonzalez & Gonzalez, 1949; Ottsen, 1985; Haseeb *et al.*, 2008), antibodies induced against the parasite antigens might be cross-reactive/destructive to the host cells, leading to decreased haemoglobin concentration (Musehel, 1966).

Some studies reported a lack of association between ABO blood type and prevalence of helminth infection (Gabr & Mandour, 1991; Cooper *et al.*, 1993; Degarege *et al.*, 2014). This could be due to the nature of the study participants. The study by Gabr & Mandour (1991) and Degarege *et al.* (2014) involved patients who might be immunologically compromised, and the study by Cooper *et al.* (1993) was conducted among adults, who might have a stronger immune status than children. As a result, the effect of ABO blood type on helminth infection might have been underestimated. In addition, variation in socioeconomic and other genetic factors (such as human leucocyte antigen, glyoxalase I system) that may affect an individual's susceptibility for helminth infection may contribute to the unseen difference in the risk of helminth infection between the different blood types in previous studies (Gabr & Mandour, 1991; Cooper *et al.*, 1993; Degarege *et al.*, 2014). Furthermore, a small sample size ($n = 148$) might also have resulted in the absence of significant difference in prevalence of helminth infection across different blood types (Gabr & Mandour, 1991).

In the present study, although the effects of age, sex, multiple infection and nutritional status on helminth infection and related anaemia were taken into consideration, the familial relationship or household condition and genetic factors such as human leucocyte antigen and glyoxalase I system, which could affect helminth infection and related morbidity, were not examined. In addition, only seven children were infected with *T. trichiura*. Thus, the current study was not powered to identify the true differences in prevalence and intensity of *T. trichiura* infection across the different blood types.

In conclusion, these findings suggest that children with blood type A are at increased risk of helminth infection, especially hookworm, and related reduction in haemoglobin level. There is a need to investigate the mechanisms by which blood type A could lead to a high risk of helminth infection and related reduction in haemoglobin level.

Acknowledgements

We would like to express our gratitude to the school communities of Tikur Wuha Elementary School for their collaboration during data collection. We also gratefully acknowledge the cooperation of the study participants.

Financial support

This work received financial support from Aklilu Lemma Institute of Pathobiology (grant number 6223).

Conflict of interest

None.

Ethical standards

Ethical approval for the study was obtained from the Institutional Review Board of Aklilu Lemma Institute of Pathobiology.

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