

Intestinal Parasite Burden and Pre-Departure Treatment Compliance in Kentucky Refugee Children: A Descriptive Study

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Abstract

Objective: Children are ½ of the world's refugees and often have intestinal parasites. This study seeks to determine the intestinal burden and pre-departure treatment of Kentucky pediatric refugees. **Methods:** This is a chart review of Kentucky pediatric refugee health screening data from 2012-2017. Stool culture results from children arriving through refugee camps were compared to non-camp children. They were placed into 3 regional groups and analyzed based on CDC pre-departure treatment recommendations.

Results: Of the 3,199 records, 1,653 had stool testing. 354 (51%) refugee camp children tested positive compared to 326 (33.9%) non-camp children. *Giardia* and *Blastocystis* were most commonly identified. Treatment aligned with CDC guidelines 64.7% of the time. CDC compliance was 83%, 79.8%, and 30.2% from Regions 1, 2, and 3 respectively.

Discussion: Pre-departure treatment of pediatric refugees needs improved compliance with CDC recommendations through education of refugee camp workers. *Giardia* and *Blastocystis* are common and metronidazole is recommended for symptomatic children.

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Background

Historically, the United States has resettled more than 50,000 refugees per year, half of whom are under 18 [1-3]. Although this number has decreased significantly over the past two years, refugees continue to arrive from either their country of origin or a refugee camp in another country, typically in the same region of the world as their country of origin. The state of Kentucky has resettled over 15,000 refugees since 2012 [1]. The most common countries of origin for refugees entering Kentucky over the last several years have been Cuba, Iraq, Somalia, Burma/Myanmar, Democratic Republic of Congo, and Bhutan-Nepal [1]. Refugee populations are a vulnerable and medically disenfranchised group in both their countries of origin and resettlement. As no centralized database for the collection and storage of refugee health data exists, individual states are tasked with the development and maintenance of refugee health data at the time of resettlement. The Kentucky Office for Refugees and the University of Louisville Global Health Center work together to perform the domestic health screenings of Kentucky's newly arrived refugees.

The Centers for Disease Control and Prevention (CDC) oversees mandated health screenings in accordance with the Refugee Act of 1980 [4]. At least 1/3 of the world's population is infected with parasites, making this a common condition in refugees resettled in the United States (US) [1, 3, 5, 6].

These infections may be subclinical and can be associated with substantial morbidity, including anemia, malnutrition, small bowel obstruction, growth restriction, periportal hypertension, hyperinfection syndrome and possible cognitive impairment in children if not treated [2, 6]. In May 1999, the CDC initiated pre-departure treatment programs for intestinal parasites, which began with a single dose of Albendazole within 3 days of departure to the US for all non-pregnant refugees over the age of 2 [4, 5, 7]. In addition to Albendazole, the guidelines expanded in 2005 to include treatment for Strongyloidiasis (Ivermectin) in refugees from Asia, the Middle East, and non-Loa Loa endemic African countries and treatment for Schistosomiasis (Praziquantel) in refugees from sub-Saharan Africa [4, 5, 7, 8]. Children are a special population because no presumptive anti-helminth treatment is recommended in those under 12 months of age and there are limitations to the use of Praziquantel and Ivermectin [2, 4, 9]. It is expected that pediatric refugees who arrive from a refugee camp would be more likely to receive appropriate pre-departure treatment because they are in a more controlled setting and as a result of the treatment, less likely to have intestinal parasites on their intake examinations. However, it is unclear and not previously documented if the suboptimal living conditions with close exposure to others from various regions change the intestinal parasite diaspora in this group [5].

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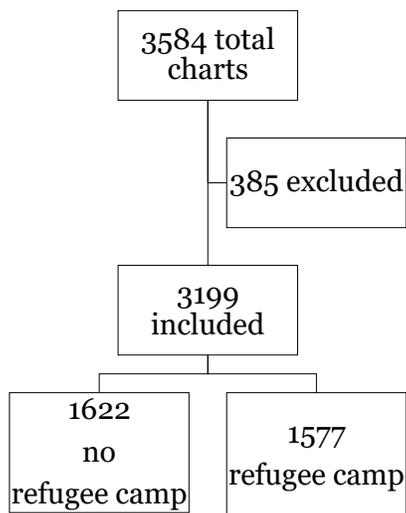


Figure 1 Overall review of the Kentucky refugee data included in the data analysis

The objectives of this study were to characterize and compare the intestinal parasite infection profiles and pre-departure treatment of Kentucky pediatric refugees who arrived from traditional refugee camps with those who did not arrive through a refugee camp. The authors will also describe the compliance of pre-departure treatment to the CDC recommendations in this population.

Methods

In 2012, the Kentucky Office of Refugees, in collaboration with the University of Louisville Global Health Center, created a secure database which stored the data from all domestic health screenings of refugees entering Kentucky. This database was kept in the REDCap platform (Developed at Vanderbilt University Institute for Clinical and Translational Research; Nashville, TN) and maintained by the University of Louisville Global Health Center. Information pertaining to refugee care, specifically pre-departure anti-helminth treatment, prior to entry into the US is also maintained within the database and is provided directly from the CDC's Electronic Disease Network (EDN), which is a centralized electronic reporting system that notifies US state and local health departments as well as screening clinics of the arrival of refugees and immigrants with medical conditions requiring follow-up [15]. The investigators received permission from the University of Louisville Institutional Review Board (IRB) to review charts from the REDCap database for this study.

This is a retrospective, descriptive study of patient charts in the REDCap database from September 1, 2012 to September 1, 2017. All refugees < 18 years of age and not pregnant at the time of treatment were included in the analysis of the parasite profiles. Refugees without any documentation pertaining to their previous residence within or outside of traditional refugee camps were excluded from all analyses. In addition, refugees with known cysticercosis or an unexplained seizure disorder were excluded through the CDC's Albendazole-treatment protocol because of the risk of adverse neurological effects from a cytotoxic agent[4].

Table 1 Country of Origin and refugee camp status in Kentucky pediatric refugees

Country of Origin	Refugee Camp	No Refugee Camp	Total
Dem. Rep. of the Congo	628	239	867
Somalia	409	143	552
Myanmar	158	218	376
Iraq	5	371	376
Bhutan	274	1	275
Syria	20	234	254
Cuba	0	242	242
Afghanistan	5	70	75
Sudan	18	20	38
Burundi	28	3	31
Pakistan	0	25	25
Eritrea	4	18	22
Rwanda	11	4	15
Ethiopia	3	4	7
Sri Lanka	0	7	7
Ukraine	0	7	7
Kenya	4	0	4
Ivory Coast	0	4	4
Saudi Arabia	0	4	4
Tanzania	3	0	3
Lebanon	0	3	3
Thailand	2	0	2
Kuwait	0	2	2
Central African Republic	1	0	1
Ghana	1	0	1
Nepal	1	0	1
North Korea	1	0	1
Turkey	1	0	1
Angola	0	1	1
Iran	0	1	1
Jordan	0	1	1
Total	1577	1622	3199

The patient charts were grouped based on the region of the world from which they originated which was documented in their immigration/refugee records. The CDC groups the countries of origin into 3 major regions based on previous epidemiologic information about the endemic intestinal parasites: Middle East, Asia, North Africa, Latin America, and the Caribbean (Region 1); Central and Southern African countries not endemic for Loa Loa (Region 2); Central and Southern African countries endemic for Loa Loa (Region 3)[4]. The recommendation for pre-departure treatment for refugees from Region 1 is single dose Albendazole and Ivermectin; Region 2 is single dose Albendazole, Ivermectin, Praziquantel; Region 3 is single dose Albendazole and Praziquantel [4]. Additionally, the recommendations consider the safety profile of each medication, particularly in children. Praziquantel is not recommended for children < 4 years of age while Ivermectin is not recommended for children < 15 kilograms(kg). The CDC does not recommend presumptive therapy in children < 12 months of age [2, 4].

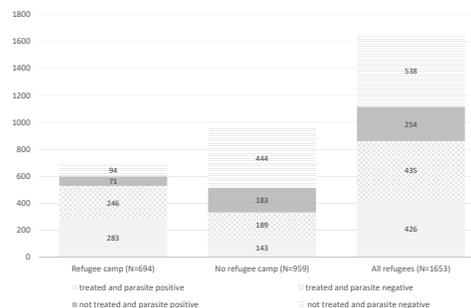


Figure 2 The distribution of the results of stool studies of Kentucky pediatric refugees

Table 2 Types of parasites detected in the stool culture results of pediatric refugees from the different world regions defined by the CDC

Stool culture results	Region 1 N (%)	Region 2 N (%)	Region 3 N (%)
Blastocystis	152 (49.8)	78 (44.1)	117 (59.1)
Giardia	55 (18)	44 (24.9)	27 (13.6)
Giardia, Blastocystis	17 (5.6)	24 (13.6)	27 (13.6)
Other nonpathogenic parasites	17 (5.6)	15 (8.5)	13 (6.6)
Dientamoeba and Blastocystis	18 (5.9)	3 (1.7)	4 (2)
Dientamoeba	15 (4.9)	3 (1.7)	0
Entamoeba histolytica	7 (2.3)	0	6 (3)
Entamoeba histolytica, Blastocystis	8 (2.6)	0	1 (0.5)
Hymenolepis, Blastocystis	3 (1)	3 (1.7)	0
Dientamoeba, Giardia, Blastocystis	3 (1)	1 (0.6)	1 (0.5)
Entamoeba histolytica, Giardia	3 (1)	0	0
Dientamoeba, Giardia	1 (0.3)	1 (0.6)	0
Entamoeba histolytica, Dientamoeba	1 (0.3)	0	0
Trichuris, Dientamoeba	1 (0.3)	0	0
Strongyloides	1 (0.3)	0	0
Giardia, Blastocystis, Hymenolepis	1 (0.3)	0	0
Dientamoeba, Hymenolepis, Blastocystis	1 (0.3)	0	0
Ascaris, Giardia	1 (0.3)	0	0
Hymenolepis	0	1 (0.6)	0
Tapeworm, Blastocystis	0	1 (0.6)	0
Trichuris	0	0	1 (0.5)
Giardia, Trichuris, Blastocystis	0	1 (0.6)	1 (0.5)
Trichuris, Blastocystis	0	1 (0.6)	0
Giardia, Tapeworm, Blastocystis	0	1 (0.6)	0
Total	305	177	198

The results of stool cultures were compared between those who arrived through a refugee camp and those who did not. The 3 regional subgroups were used evaluate potential trends in parasite diaspora based on region and refugee camp status. The records were reviewed to determine if the included pediatric refugees received appropriate pre-departure treatment for intestinal parasites as outlined by the CDC. Children < 4 years of age were excluded from this analysis because of the anti-helminth restrictions in the younger and smaller weight individuals. The stool pathology was described for those who received appropriate pre-departure treatment and those who did not. It was further described within the 3 regional groups and refugee camp status.

A sensitivity analysis was conducted using the refugees < 4 years of age and < 12 months of age to determine the appropriateness of treatment and determine if they had different intestinal parasite profiles compared to those 4 years of age and older. The descriptive analysis of all the data was performed using IBM SPSS version 21.

Results

There were 3,584 pediatric refugee charts reviewed from 9/1/2012 to 9/1/2017. 385 were excluded because the records were missing information about refugee camp stay prior to immigration into Kentucky, resulting in 3,199 pediatric refugee records (**Figure 1**). There were 686 (21.4%) pediatric refugees < 4 years of age and 57 (1.8%) < 12 months of age. Kentucky pediatric refugees most commonly came from The Democratic Republic of the Congo (**Table 1**).

Upon arrival, there were 1,653 children who had stool studies results (**Figure 2**). There were 680 children that had abnormal stool studies and 426 (62.6%) received pre-departure therapy prior to arrival in the US. In children who did not spend any time in a camp and had stool studies, 326 (33.9%) had intestinal parasites in their stool. In children who spent time in refugee camps and were tested, 354 (51%) were found to have parasites in their stool (**Figure 2**). In children who arrived to Kentucky from refugee camps and did not receive pre-departure treatment, the incidence of intestinal parasites was 71 out of 165 (43%).

Overall, pre-departure anti-helminth therapy in refugees > 4 years of age was appropriate based on CDC recommendations

Table 3 Kentucky refugee children who received appropriate anti-helminth treatment based on the CDC recommendations prior to arrival in the United States

Refugee Population	Refugee camp	No refugee camp	Total
Region 1. Asia, Middle East, North Africa, Latin American, & Caribbean	86.7%	80%	83%
Region 2. Sub-Saharan Africa, non-Loa loa-endemic area	85.4%	56.4%	79.8%
Region 3. Sub-Saharan Africa, Loa loa- endemic area	22.5%	50.3%	30.2%
Total	61.7%	69.8%	64.7%

64.7% of the time. There were only 6 total cases of soil helminths, 1 case of Strongyloides and no cases of Schistosomiasis. The most common parasites found in refugee children from all three regions were *Blastocystis* and *Giardia* (**Table 2**). The pediatric refugees from this Region 1 were treated based on CDC guidelines 83% of the time (**Table 3**). There were 75 patients who arrived from Afghanistan. None of these patients received presumptive treatment regardless of refugee camp status and the most common organisms identified were also *Giardia* (18%) and *Blastocystis* (18%). Ascaris was present in 3% of the Afghani pediatric refugees.

The pediatric refugees from Region 2 had a 79.8% compliance rate with CDC guidelines while the pediatric refugees from Region 3 had 30.2% compliance (**Table 3**). The CDC recommends that these individuals from Region 3 should have Ivermectin added based on the results of stool studies. However, if children who received all three as presumptive treatment were included in the “appropriate treatment” category, then compliance would be 85.5% for region 3 and 83.1% for all pediatric Kentucky refugees.

These results were further analyzed and grouped into children who were previously in a refugee camp and those who were not. Overall, in pediatric refugees previously in a refugee camp, they received appropriate presumptive intestinal parasite treatment 61.7% of the time (**Table 3**). The most common parasites found children previously in refugee camps from each of the three regions were Blastocystosis and *Giardia* (**Figure 3**). Based on the CDC recommendations by region, the children in Region 1 had 86.7% compliance, Region 2, 85.4% compliance, and Region 3, 22.5% compliance (**Table 3**). If children in Region 3 who received all three medications were included in the “appropriate treatment” category, then compliance would be 88.4% for Region 3 and 86.9% for all pediatric Kentucky refugees who were previously in refugee camps.

Overall, in pediatric refugees not previously in a refugee camp, they received appropriate presumptive therapy 69.8% of the time (**Table 3**). The most common parasites found in refugee children not previously in camps from each of the three regions were Blastocystosis and *Giardia* (**Figure 3**). Based on the CDC recommendations by region, the children in Region 1 had 80% compliance, Region 2, 56.4% compliance, and Region 3, 50.3% compliance (**Table 3**). If children in Region 3 who received all three medications were included in the “appropriate treatment” category, then compliance would be 78.3% for Region 3 and 76.7% for all pediatric Kentucky refugees who were not previously in refugee camps.

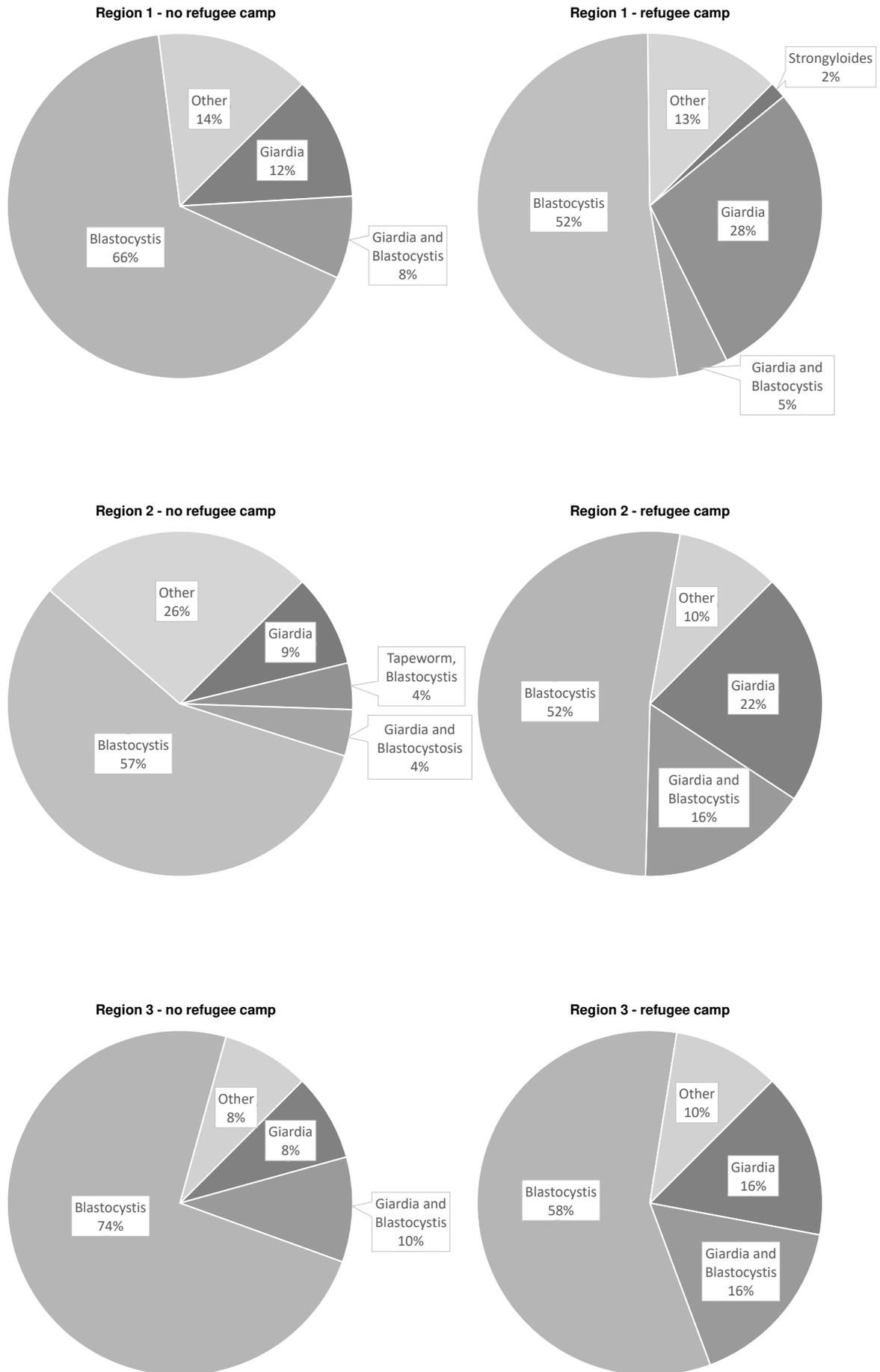


Figure 3 The most common intestinal parasites by region and history of refugee camp exposure

An analysis was conducted looking at pediatric refugees < 4 years of age and < 12 months to determine if they were inappropriately receiving anti-helminth treatment and if their stool culture results were different from the remainder of the charts reviewed. In children < 4 years, pre-departure treatment was given in 416 patients. There were 37 (8.8%) patients who received Praziquantel, which is not approved in this group. 32 of these children arrived through a refugee camp. There were 65 refugees < 4 years who were given Ivermectin. 47 (72.3%) of these patients were under 15 kg and therefore should not have received it. Seven of the children < 15 kg who received Ivermectin arrived through a refugee camp. In summary, there were 20.1% of children who received Praziquantel or Ivermectin despite contraindications based on age and weight. 46.4% of these children arrived through a refugee camp.

There were 354 refugees < 4 years who were tested for intestinal parasites. 92 had positive stool studies on evaluation, 51 of which received pre-departure treatment. The most common organisms were *Giardia* and *Blastocystis* and there were no cases of soil helminths, Schistosomiasis, or Strongyloides.

There were 11 (17.4%) refugee children < 12 months of age who received pre-departure treatment for intestinal parasites despite the CDC recommendations. Forty (of the total 63) children < 12 months of age were tested for intestinal parasites and 3 had positive stool cultures, which resulted *Giardia* and/or *Blastocystis*. None of the 3 refugee children < 12 months of age who had positive stool cultures received pre-departure treatment.

Discussion

The current CDC guidelines for pre-departure treatment of intestinal parasites in refugees were designed to specifically address infections with soil transmitted helminths, Strongyloides, and Schistosomiasis. This study supports the findings of other numerous studies performed on refugees resettling in other US and Western cities which demonstrate a low incidence of infection with these parasites while also demonstrating the persistent burden of protozoal infections, specifically *Giardia* and *Blastocystis* [4, 5, 10, 11].

The distinction between prior living environments (refugee camp vs none) has been used to explain differences in health profiles of newly arriving refugee children, however differences in intestinal parasite burden and pre-treatment medications has not been evaluated prior to this study [12]. This study demonstrated similar stool parasite profiles in pediatric refugees regardless of prior encampment status and country of origin; however, those arriving directly from refugee camps presented with higher rates of positive stool results. This is likely attributed to irregular access to preventive health services, insufficient sanitation facilities and hygiene practices, and higher likelihood of transmission rates of communicable illness particularly among children living in poor housing and close quarters conditions [12].

Children who arrived through refugee camps had a lower compliance with CDC recommendations for pre-departure therapy compared to those who did not arrive through refugee camps; however, this appears to be skewed by Region 3. Refugees arriving through camps from Regions 1 and 2 had a

high compliance with CDC recommendations with appropriate pre-departure treatment rates of 86.7% and 85.4% respectively, while Region 3 compliance was low. The guidelines recommend refugees from Region 3 receive Albendazole and Praziquantel but many of the Kentucky pediatric refugees received triple-therapy with Albendazole, Praziquantel, and Ivermectin [4]. While overtreatment in this group should not increase parasite burden as identified by stool studies, it unnecessarily increases the risk of encephalopathy associated with a high load of dying microfilaria in an established Loa Loa endemic region [4, 9]. Therefore, the CDC guidelines should be more closely adhered to in this group of individuals as originally designed. Based on these findings, education initiatives focused on health care workers working in refugee camps located in countries endemic for Loa Loa are recommended to improve the adherence to the CDC guidelines for pre-departure parasite treatment.

This study additionally found that there was inappropriate pre-departure treatment of young children. 86% of the children < 4 years of age who received Praziquantel and 14.9% of children < 15 kg who received Ivermectin arrived through a refugee camp. The American Academy of Pediatrics warns against the use of Ivermectin in children under 2 years of age and under 15 kg because they have a less developed blood brain barrier and therefore have a higher risk of central nervous system side effects, namely encephalopathy [9]. The culture results in children < 4 and those < 12 months are similar to children in the overall study population and didn't show an increase in soil helminths, Strongyloides, or Schistosomiasis in the children who did not receive pre-departure therapy. These findings further support the need to improve adherence to the guidelines set forth by the CDC, through awareness, education, and treatment coordination among refugee camp healthcare workers, since presumptive therapy will not provide any added benefit in these populations but will increase the number of possible adverse effects.

This study showed *Giardia* and *Blastocystis* as the major stool pathogens in Kentucky pediatric refugees. It has been debated whether *Blastocystis* is a pathogenic organism; however, some suggest to treat if a patient is symptomatic and has no other identifiable organism in the stool [13]. *Giardia* can cause diarrhea, malaise, abdominal cramping, nausea, weight loss, and failure to thrive [9]. At this time, treatment of symptomatic individuals is recommended to prevent infection and hasten the resolution of symptoms; however, the illness is typically self-limiting. Currently, the stool of pediatric Kentucky refugees is only tested if symptomatic and therefore would warrant treatment. There are many individuals who are asymptomatic and have *Giardia* in their stool. These patients only require treatment if there is an increased risk of transmission to others [9, 14]. This includes children who attend daycare/school, live at home with an immunocompromised individual, live at home with a pregnant woman, or handle food [9]. Unfortunately, many of the Kentucky pediatric refugees will fall into this group and require treatment even if they are asymptomatic. Albendazole daily for 5 days or Metronidazole 3 times daily for five days can be used to treat *Giardia* infections in any age individual [14]. Although Albendazole is more convenient at once daily, Metronidazole is a more cost-effective treatment in the US. In addition, Metronidazole would be an appropriate treatment for *Blastocystis* in the setting of symptomatic illness and absence of other causative organisms [13].

The authors recommend the initiation of treatment with Metronidazole promptly in symptomatic refugee children who have received appropriate pre-departure treatment. Screening studies can take several days to weeks and this would provide antimicrobial coverage for *Giardia* and *Blastocystis* and therefore, prevent the spread of infection in a population where follow up and language barriers can challenge the provision of appropriate treatment and healthcare.

The data for this study were obtained through a database review, therefore a limitation of the study is incorrectly inputted data into REDCap. However, a large number of charts were reviewed to offset any effect of random human error and all data gathered from pre-departure health assessments were provided directly from the CDC's EDN, which is unlikely to have incorrectly inputted data [15]. Another limitation is the lack of follow up information for those patients who had positive stool results. Because the database captured intake data, it does not have information about the treatment and follow up in those children with positive stool studies. Additionally, stool ova and parasite testing have low sensitivity for many intestinal parasites, especially if only one or two samples were submitted, therefore our measurement of parasite burden likely underestimates the true prevalence of intestinal parasites within our clinical samples. Lastly, refugees provided stool studies if they were symptomatic upon arrival or if they presented to their initial screening visits with incomplete records of pre-departure treatment. Therefore, we cannot evaluate the positive predictive value of stool testing in our study population as we cannot differentiate those who underwent stool studies due to symptoms and those who did not present with adequate information to their initial screening visit.

In conclusion, there is high compliance to the CDC recommendations for presumptive treatment of intestinal parasites in Kentucky pediatric refugees from Regions 1 and 2. Refugees from region 3 are inappropriately given Ivermectin which can cause encephalopathy in patients in this high risk group and interventions should be focused on improving compliance with CDC recommendations in this group and in young children (< 4 years). Early initiation of Metronidazole in symptomatic pediatric refugees should be considered to prevent the spread of protozoal infection upon resettlement.

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