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Role of seasonal variation on the prevalence and risk factors of trichuriasis among the aboriginal community in Malaysia

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Article info	Summary
Received April 22, 2020 Accepted December 31, 2021	<i>Trichuris trichiura</i> is a soil-transmitted helminth prevalent in developing countries with poor, inade- quate sanitation and unsafe water sources. In Malaysia, the prevalence of trichuriasis is relatively high among the aboriginal community due to poverty and poor sanitation. However, there are few studies to determine the seasonal variation on the prevalence and risk factors to acquire <i>Trichuris</i> <i>trichiura</i> infection in Malaysia. The present study found higher <i>Trichuris trichiura</i> infection during the dry season (63.6%; 138/217) in comparison to the wet season (55.5%; 142/256). Low house- hold income, low education level and practice of open defecation were significant risk factors to acquire <i>Trichuris trichiura</i> infection during the wet season. Usage of untreated water supplies for daily activities was a risk factor to acquire trichuriasis during the dry season. This study highlighted that poverty and poor sanitation practices as well as drinking untreated water put the aborigines at high risk to acquire trichuriasis. Therefore, health education, improved sanitation and provision of treated water supply are recommended for the prevention and control of <i>Trichuris trichiura</i> infections in the aboriginal community. Keywords: <i>Trichuris trichiura;</i> low socio-economy; open defecation; untreated water; aborigines; season

Introduction

Trichuris trichiura, also known as whipworm, is one of the most common soil-transmitted helminths affecting rural and poor communities especially in tropical countries. The infection has been associated with anemia and undernutrition (Freeman *et al.*, 2016). The infection is also attributed to lack of sanitation, sources of poor drinking water and poor hygiene (Adu-Gyasi *et al.*, 2018). Similar to other soil-transmitted helminth infections, trichuriasis is associated with poor socioeconomic conditions including low education level, low household income and poor access to sanitation facilities and clean drinking water (Campbell *et al.*, 2016).

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Although the clinical consequences associated with the infection may not pose a major problem, the prevalence of the infection is still high, therefore it is still of public health concern in Malaysia. In addition, it is common in low-income communities including the aborigines, rural and poor Malay community, children in estates and squatter areas (Anuar *et. al.*, 2014).

Development of *T. trichiura* ova requires optimum temperature and moisture. Transmission of *T. trichiura* ova is via accidental consumption of egg-contaminated food or drinks (Anuar *et. al.*, 2014). Malaysia is a country with tropical weather and due to the proximity to water, the climate of Malaysia is often humid. As a result of this, Malaysia has the optimum climate for the embryonation of

T. trichiura ova. In Malaysia, the infection is still endemic among rural communities, particularly the aborigines (Muslim *et al.*, 2019). Although there are many epidemiological studies associated with *T. trichiura* infection among the poor communities in Malaysia, there is an absence of studies that determine the seasonal variation in the prevalence and risk factors of *T. trichiura* infections. To the best of our knowledge, this is the first study to identify the prevalence and risk factors of *T. trichiura* infections in the aboriginal community during two seasons in Malaysia.

Materials and Methods

Study area and study design

A cross-sectional study was performed by collecting of stool samples from the aboriginal community (n=473) residing at three aboriginal villages in Kuala Krau, Temerloh, Pahang during two seasons; wet season from October to November 2014 (n=256) and dry season in June 2015 (n=217). (Fig. 1). The seasons were identified based on the data obtained from Malaysian Meteorological Department from 2010 to 2013, recorded at Temerloh station. The sample size was calculated using Epi Info based on study by Anuar *et al.* (2021), with 95 % confidence level and an 80 % power. The minimum sample size required was 441.

Questionnaires

The objectives and protocol of the study were explained briefly to the participants and family members. An adapted structured questionnaire in the Malay language was used and explained to the subjects through an oral interview (Anuar *et al.,* 2014). The guardians or parents who signed the informed consent for their children were briefed on the details related to the study.

Risk factors for *T. trichiura* infections were determined using the data of questionnaires including the profile of participants, environmental sanitation and source of water, personal hygiene and habits, exposure to animals and educational background of the parents. Meanwhile, the outcome of trichuriasis was determined using data regarding the signs and symptoms of *T. trichiura* infections.

Stool collection and helminth identification

Labeled stool containers were distributed to participants a day prior to stool collection. Approximately 10 grams of stool collected from the participants were subjected to preservation in polyvinyl alcohol (PVA). The preserved stool was filtered into a centrifuge tube. After centrifugation, the supernatant was decanted. Stool sample was then collected using a fine hair brush and smeared on a cover slip and air-dried, followed by Wheatley's Trichrome staining (Salleh *et al.*, 2012). The stained slides were examined with microscope using 100x magnification for *T. trichiura* ova (Nikon eclipse E100).

Statistical analysis

Data were entered into the Statistical Package for Social Sciences software for Windows (SPSS Version 23, Chicago, IL, USA). Prevalence of *T. trichiura* infections during both wet and dry seasons were calculated using descriptive analysis.



Fig. 1. Map of the aboriginal villages in Kuala Krau Pahang.

Table 1. Prevalence and significant differ	ence of Trichuris trichiura infection	s during the wet and dry seasons.
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W	et season (n=25	6)		Dry season (n=21	7)	Significant difference between the two seasons		
Number of infections	Prevalence (%)	95 % CI	Number of infections	Prevalence (%)	95% CI	Z-score	<i>p</i> -value	
142	55.5	49.2, 61.7	138	63.6	56.8, 70.0	1.792	0.073	

Chi-square (χ 2) analysis was used to determine the associations between the prevalence of *T. trichiura* infection and the independent variables. The factors significantly associated with *T. trichiura* infections in the chi-square analysis were included in a logistic regression analysis for the identification of risk factors for *T. trichiura* infections. The level of statistical significance was deemed at *P* < 0.05. All significant risk factors were computed for odds ratio (OR) and 95 % confidence interval (CI) in the multivariate analysis. The significant difference of the prevalence of *T. trichiura* infections between wet and dry seasons was analyzed by proportionate test at *P* < 0.05.

Ethical Approval and Informed Consent

The study protocol was approved by Research and Ethical Committee, Faculty of Medicine, Universiti Kebangsaan Malaysia (FF-2014-219) prior to stool samples collection. Permission for fieldwork was granted from the Department of Orang Asli Development (JAKOA) (JAKOA/PP.30.032JId29(04)). Prior to the study, informed consent was obtained from all participants and from the parent or guardian (for participants aged 16 years old and below)

Results

Prevalence and risk factors of T. trichiura infection

Higher prevalence of *T. trichiura* infections was observed in the dry season (63.6 %; 138/217) in comparison to the wet season (55.5 %; 142/256). However, the difference of the prevalence of *T. trichiura* infections between the two seasons was statistically insignificant (p>0.05) (Table 1).

Chi square (χ 2) analysis revealed that low household income of RM500 and below [OR=1.511(1.294, 3.891), *p*=0.017], low educational background [OR=1.451(1.266, 5.764), *p*=0.003], untreated water supply [OR=1.857(1.105, 3.120), *p*=0.019] and practice of open defecation [OR=1.737(1.043, 2.893), *p*=0.033] were the risk factors significantly associated with *T. trichiura* infections among the aborigines during the wet season. Meanwhile, age of less than 15 years old [OR=1.496(1.283, 3.869), *p*=0.014], occupation as farmers and rubber tappers [OR=1.788(1.005, 3.180), *p*=0.047], untreated water supply for daily activities [OR=2.154(1.219, 3.807), *p*=0.008] and practice of open defecation [OR=2.120(1.203, 3.736), *p*=0.009] were the significant risk factors associated with trichuriasis during the dry season (Table 2).

Multivariate analysis confirmed that low household income of RM500 and below [OR=1.545(1.304, 3.979), p=0.042], low educational background [OR=1.440(1.195, 2.997), p=0.049] and practice of open defecation [OR=2.740(1.184, 6.339), p=0.019] were the significant predictors for trichuriasis during the wet season and untreated water supply for domestic activities [OR=2.253(1.996, 5.095), p=0.049] was the only significant risk factor to acquire trichuriasis among the aboriginal community during the dry season (Table 3).

Symptoms associated with T. trichiura infection

Gastrointestinal symptoms including abdominal pain, diarrhea, flatulence and nausea were not associated with *T. trichiura* infection (p>0.05). The symptoms could be due to other infections.

Other intestinal parasites

Besides *T. trichiura*, several other intestinal parasites were also detected in the stool including *Ascaris lumbricoides* (31.6 % during wet season and 24.9 % during the dry season), *Giardia lamblia* (20.7 % during wet season and 8.3 % during the dry season), *Entamoeba* spp. (21.9 % during wet season and 24.4 % during the dry season), *Blastocystis* spp. (21.5 % during wet season and 17.5 % during the dry season), *Chilomastix mesnili* (0.8 % during wet season and 0.5 % during the dry season), *Dientamoeba fragilis* (0.8 % during wet season and 0.0 % during the dry season), *Endolimax nana* (8.2 % during wet season and 3.2 % during wet season and 2.3 % during the dry season) and *Iodamoeba butschlii* (4.3 % during wet season and 3.2 % during the dry season) (Table 4).

Ascaris lumbricoides infection was associated with *T. trichiura* infection during both wet (χ^2 = 32.460, p<0.001) and dry seasons (χ^2 = 22.882, p<0.001). Similarly, hookworm infection was also found to be associated with *T. trichiura* infection during both wet (χ^2 = 23.614, p<0.001) and dry seasons (χ^2 = 27.544, p<0.001). Meanwhile, *Giardia lamblia* infection was associated with *T. trichiura* infection only during the dry season (χ^2 = 8.069, p=0.005) (Table 4).

Discussion

Soil-transmitted helminth (STH) infections are important neglected tropical diseases which cause diarrhea, growth retardation, iron deficiency anemia and cognitive impairment. In Malaysia, among all the STH, infection with *T. trichuria* is the most common,

Variablee	Wot coses	(95C=u) uu	Dmy coo	eon (n=217)	OR	(95% CI)	v-d	alue
valiables					Wet season	Dry season	Wet	Dry
	Prevalence	(95% CI)	Prevalence	(95% CI)				
Age ≤15 ≻15	58; 22.7 % 84; 32.8 %	17.7, 28.3 27.1, 38.9	53; 24.4 % 85; 39.2 %	18.9, 30.7 32.6, 46.0	1.690 (1.420, 2.135) 1	1.496 (1.283, 3.869) 1	0.143	0.014*
Gender Female Male	77; 30.1 % 65; 25.4 %	24.5, 36.1 20.2, 31.2	63; 29.0 % 75; 34.6 %	23.1, 35.6 28.3, 41.3	1.994 (1.606, 2.630) 1	0.703 (0.404, 1.225) 1	0.980	0.213
Number of household members ≥8 <8	93; 36.3 % 49; 19.1 %	30.4, 42.6 14.5, 24.5	78; 35.9 % 60;27.7 %	29.6, 42.7 21.8, 34.1	1.967 (1.544, 3.718) 1	1.722 (1.412, 2.265) 1	0.909	0.255
Monthly household income ≤ RM500 > RM500	90; 35.2 % 52; 20.3 %	29.3, 41.4 15.6, 25.8	88; 40.6 % 50; 23.0 %	34.0, 47.4 17.6, 29.2	1.511 (1.294, 3.891) 1	1.021 (1.575, 1.813) 1	0.017*	0.944
Education level No formal education Primary and secondary education	37; 14.5 % 105; 41.0 %	10.4, 19.4 34.9, 47.3	40; 18.4 % 98; 45.2 %	13.5, 24.2 38.4, 52.0	1.451 (1.266, 5.764) 1	1.935 (1.511, 2.712) 1	0.003**	0.828
Occupation Rubber tapper, farmer Professional, factory	140; 54.7 % 2; 0.8 %	48.4, 60.9 0.1, 2.8	97; 44.7 % 41; 18.9 %	38.0, 51.6 13.9, 24.8	3.889 (1.770, 9.648) 1	1.788 (1.005, 3.180) 1	0.078	0.047*
Water supply Untreated tap water from river and wells Governmental tap water	101; 39.5 % 41; 16.0 %	33.4, 45.7 11.8, 21.1	95; 43.8 % 43; 19.8 %	37.1, 50.7 14.7, 25.8	1.857 (1.105, 3.120) 1	2.154 (1.219, 3.807) 1	0.019*	0.008**
Usage of stored river water Yes No	75; 29.3 % 67; 26.2 %	23.8, 35.3 20.9, 32.0	60; 27.7 % 78; 35.9 %	21.8, 34.1 29.6, 42.7	1.539 (1.937, 2.530) 1	1.072 (1.613, 1.876) 1	0.088	0.807

Table 2. Univariate analysis of the risk factors associated with Trichturis trichtura infections in the aboriginal community during wet (n=256) and dry (n=217) seasons.

Latrine system/ defecation No latrine system, river Flush toilet and pit latrine	140; 54.7 % 2; 0.8 %	48.4, 60.9 0.1, 2.8	135; 62.2 % 3; 1.4 %	55.4, 68.7 0.3, 4.0	1.892 (1.311, 11.519) 1	1.022 (0.997, 1.048) 1	0.482	0.187
Wash hand after playing with soil No Yes	16; 6.3 % 126; 49.2 %	3.6, 10.0 42.9, 55.5	9; 4.2 % 129; 59.4 %	1.9, 7.7 52.6, 66.0	0.907 (0.423, 1.947) 1	0.543 (0.206, 1.430) 1	0.802	0.211
Wash hand after defecation No Yes	7; 2.7 % 135; 52.7 %	1.1, 5.6 46.4, 59.0	5; 2.3 % 133; 61.3 %	0.8, 5.3 54.5, 67.8	1.687 (1.241, 1.955) 1	0.705 (0.184, 2.705) 1	0.480	609.0
Defecation area River, bushes Flush toilet and pit latrine	66; 25.8 % 76; 29.7 %	20.5, 31.6 24.2, 35.7	67; 30.9 % 71; 32.7 %	24.8, 37.5 26.5, 39.4	1.737 (1.043, 2.893) 1	2.120 (1.203, 3.736) 1	0.033*	0.009**
Animals rearing Yes No	89; 34.8 % 53; 20.7 %	28.9, 41.0 15.9, 26.2	81; 37.3 % 57; 26.3 %	30.9, 44.1 20.5, 32.7	1.621 (1.983, 2.674) 1	1.968 (1.551, 2.698) 1	0.058	0.908
Educational status of father No formal education Primary and secondary education	67; 26.2 % 75; 29.3 %	20.9, 32.0 23.8, 35.3	41; 18.9 % 97; 44.7 %	13.9, 24.8 38.0, 51.6	1.591 (0.960, 2.635) 1	1.862 (1.475, 2.561) 1	0.071	0.623
Educational status of mother No formal education Primary and secondary education	62; 24.2 % 80; 31.3 %	19.1, 29.9 25.6, 37.3	39; 18.0 % 99; 45.6 %	13.1, 23.7 38.9, 52.5	1.434 (1.863, 2.383) 1	1.021 (0.551, 1.890) 1	0.164	0.948

* significant at ρ <0.05 ** significant at ρ <0.01

Table 3. Multivariate analysis of the risk factors of Trichuris trichiura infections in the aboriginal community during wet (n=256) and dry (n=217) seasons.

Verichlee	OR	(95% CI)	<i>p</i> -value		
variables	Wet season	Dry season	Wet	Dry	
Age ≤15	NA	1.317 (1.396, 4.381)	NA	0.653	
Monthly household income ≤ RM500	1.545 (1.304, 3.979)	NA	0.042*	NA	
Education level No formal education	1.440 (1.195, 2.997)	NA	0.049*	NA	
Occupation Rubber tapper, farmer	NA	1.435 (1.768, 2.683)	NA	0.258	
Water supply Untreated tap water from river and wells	1.362 (1.030, 4.414)	2.253(1.996, 5.095)	0.426	0.049*	
Defecation area River, bushes	2.740 (1.184, 6.339)	1.513 (1.474, 4.834)	0.019*	0.485	
* Significant at $p \le 0.05$					

Significant at p<0.05

especially among the aboriginal community (Anuar et al., 2014). The present study indicated the overall prevalence of 59.2 % trichuriasis during both seasons which is within the range of previous prevalence studies (Anuar et. al., 2014; Muslim et al., 2019; Mohd-Shaharuddin et al., 2018). Trichuriasis has been reported to be more prevalent than other STH infections regardless of the tribal difference: Mah Meri, a sub-tribe of Senoi, and Temuan, a sub-tribe of Proto-Malay, both have similar trend of precedence of trichuriasis over the other STH infection (Chin et al., 2016). In general, the aborigines in Malaysia have experienced transition state between hunter-gatherer lifestyle towards modernity. The

government of Malaysia has demarginalized many of the aborigines by improving existing aboriginal villages and part of the aboriginal villages has been equipped with treated tap water supply. On the other hand, some aboriginal communities are still living and remaining in or near the forested areas (Muslim et al., 2019). The aborigines in the current study are of Senoi tribe and Jahut sub-tribe. They are mainly rubber tappers and farmers while the remaining are government and private sector's employees. Among the three villages of the study area, only one village, known as Kampung Penderas, is equipped with facilities such as treated tap water supply, electricity, toilets with pit latrine system,

	Number of i	nfection (%)	Association with T. trichiura infections				
Intestinal parasites	Wet season	Dry season	Wet seaso	on (N=256)	Dry sease	on (N=217)	
-	(N=256)	(N=217)	X ²	<i>p</i> -value	X ²	<i>p</i> -value	
Ascaris lumbricoides	81 (31.6 %)	54 (24.9 %)	32.460	<0.001**	22.882	<0.001**	
Hookworm	59 (23.0 %)	73 (33.6 %)	23.614	<0.001**	27.544	<0.001**	
Giardia lamblia	53 (20.7 %)	18 (8.3 %)	3.430	0.064	8.069	0.005**	
Entamoeba spp.	56 (21.9 %)	53 (24.4 %)	2.412	0.120	2.267	0.132	
Blastocystis spp.	55 (21.5 %)	38 (17.5 %)	1.940	0.164	0.162	0.688	
Chilomastix mesnilii	2 (0.8 %)	1 (0.5 %)	1.618	0.203	0.575	0.448	
Dientamoeba fragilis	2 (0.8 %)	0 (0.0 %)	2.511	0.113	NA	NA	
Endolimax nana	21 (8.2 %)	7 (3.2 %)	2.359	0.125	1.529	0.216	
Entamoeba coli	10 (3.9 %)	5 (2.3 %)	2.535	0.111	0.595	0.441	
lodamoeba butschlii	11 (4.3 %)	7 (3.2 %)	0.004	0.950	1.529	0.216	

** Significant at p<0.01

NA Not applicable

primary school, road access to a small town namely the Kuala Krau and several other facilities. The other two villages, known as Kampung Terbol and Kampung Lubok Wong are lack of these facilities, except for road access to other villages and a rainwater storage tank in each village. In terms of customary cultures, only a few of the aborigines who lived in Kampung Penderas are involved in professions in the government and private sectors. Meanwhile, the others spent their days on fishing, hunting, collecting and selling rattans and farming. Despite the effort of the government and public health authorities to improve the lifestyle of some of the aborigines, particularly those with settlements at the downstream of the river, most of them are still living with their common customary cultures and belief. In terms of sanitation and hygiene, most of them still live with a lack of hygiene practices and the utilization of latrines is low. This might explain the reason why trichuriasis is still endemic in the community although many facilities are provided to some of them.

A higher prevalence of trichuriasis during the dry season might be due to heavy rainfall during wet season, which may wash away most of the *Trichuris* ova on the soil and spread the ova into the wider environment. Daily activities were restricted during the wet season due to heavy rainfall and flood. Since most of the aborigines performed their usual domestic activities which may expose them to the wider environment such as fishing, farming, hunting and others more frequently during the dry season, therefore the risk to contract trichuriasis through contaminated hands was higher.

STH infection is endemic in many parts of the world, particularly in low-income communities (Ediriweera et al., 2019). Low income has been reported to be a strong predictor of various diseases, including intestinal parasitic infections; people with low income significantly had a higher risk to be infected with intestinal parasites (Dai et al., 2019). In this study, a monthly household income of less than RM500 was found to be the significant risk factor for the aborigines to acquire trichuriasis during the wet season with the odds of 1.545. A strong association between low income and health was reported where there is a higher risk of health problems for the low-income groups in comparison with middle to higher income groups (Stronks et al., 1997). Our study found the same association; low income is associated with a higher risk to contract trichuriasis during the wet season. Most of the aborigines could not get their usual earnings during the wet season due to restrictions in movement particularly heavy rainfall and flood. Low income leads to poor medical care, poor nutrition thus increasing the exposure to harmful agents (Syme & Berkman, 1976).

Low education level has been previously suggested by various studies to be associated with soil-transmitted helminth infections (Pham-Duc *et al.*, 2013). Rural communities in Ghana with low education levels had a higher prevalence of soil-transmitted helminths infection in comparison to those with a high level of education (Adu-Gyasi *et al.*, 2018). In agreement with that, our study indicated that aborigines with low education levels had

a higher risk to contract *T. trichiura* infections in comparison to the aborigines with medium to a high level of education during the wet season. The aborigines with low education level are still involved in outdoor activities even during rainy days. Meanwhile, aborigines with medium or high education level restricted their outdoor activities due to worry of the danger and accidents that they may experience while performing various activities such as hunting, fishing, farming, playing and others during the wet season.

Open defecation is a common practice among the aborigines. In our study, we found that this practice is very common since many of the aborigines still hold on their cultural belief to perform such practice. Among the aboriginal community in this study, those who perform open defecation had a higher risk to acquire trichuriasis during the wet season with the odds of 2.740 as compared to the aborigines who defecate in a latrine. Such practice increases their chances to be exposed to many sources of infection in the environment. Besides, aborigines who perform open defecation may not practice proper handwashing after defecation. Open defecation practices among rural community in Ghana as a result of lack of toilet facilities leads to high prevalence of soil-transmitted helminths infection (Adu-Gyasi et al., 2013). A study in India found that although sanitation has been improved, however low usage of latrine among the community leads to no reduction in soil-transmitted helminths infection (Clasen et al., 2014; Patil et al., 2014). Soil moisture and relative humidity are among the factors which influence the survival of viable ova of soil-transmitted helminths (Gyawali, 2018). In our study, open defecation practice during the wet season may have spread the ova to a wider area. With optimum soil moisture and humidity, this may have contributed to infection among the aborigines during the wet season.

Utilisation of untreated water was the major risk factor that increased the transmission of intestinal parasitic infection among the aboriginal community (Chin *et. al.*, 2016). In line with that, Moktar *et al.*, (1998) reported usage of untreated water sources from well water was the risk factor for trichuriasis among aboriginal children. The present study identified usage of untreated tap water supply which originated from rivers and wells for domestic activities as a significant risk factor to acquire *T. trichiura* infection during the dry season with the odds of 2.253. Open defecation at the open field may introduce *Trichuris* ova into the water bodies such as rivers, well water and other water sources by various means, such as rainfall. Besides that, open defecation is performed at the river bench; hence the non-infective ova can become infective via exposure to the soil.

Activities such as washing, bathing and others at the river bench may introduce the infective ova into the river water. Natural water bodies especially river water are one of the most important sources of water used for daily activities within the community. As described previously, untreated tap water from the river was used daily and the river water was collected and stored in the houses by the most of the aborigines although several houses located at the downstream of the river are equipped with treated water supply (Noradilah *et al.*, 2017). Water contaminated with helminth ova pose significant public health risks where people may be infected by exposure to the contaminated water such as wastewater and sludge (Gyawali, 2018). In our study, river water contaminated with fecal materials serves as an important source of infection to the aboriginal community. Using tap water originating from the contaminated river through various activities such as cooking preparations, washing, bathing and others and consuming untreated tap water via food or drinking water put the aborigines at higher risk to contract trichuriasis during the dry season.

This study also identified an association between *T. trichiura* infection and the other STH, namely *Ascaris lumbricoides* and hookworm infection, respectively during both seasons. Since soil is required for the development of the infective egg, therefore this might explain the association between *T. trichiura* infection and the other STH in the aboriginal community. *Giardia lamblia* was also found to be associated with *T. trichiura* infection during the dry season. *Giardia* cyst is known to survive in the soil and the mode of transmission is similar for both *T. trichiura* and *Giardia* via the faeco-oral route.

This study highlighted that low socioeconomic status contributes to high prevalence of trichuriasis in the aborigines living in Kuala Krau, Temerloh, Pahang especially during the wet season. In addition, unhygienic lifestyle and behavior play important roles in the acquisition of trichuriasis. Unsafe water supply used for daily activities during the dry season puts the aborigines at high risk to contract trichuriasis. Provision of treated water supplies, health education, access to sanitation facilities and promotion of good health behavior such as high usage of a proper latrine for defecation are hoped to reduce the prevalence of trichuriasis among the aboriginal community.

Conflict of Interest

The authors declare no conflict of interest.

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