

Review Article

HOOKWORM IN STRAY CATS (*Felis silvestris catus*) AS CUTANEOUS LARVA MIGRANT AGENT (CLM) IN HUMANSFadhil Ihsan Mahendra¹, Soebaktiningsih², Risma Karlina Prabawati³¹Medical Program, Faculty of Medicine, Universitas Muhammadiyah, Malang, Indonesia²Department of Parasitology, Faculty of Medicine, Universitas Muhammadiyah, Malang, Indonesia³Department of Neurology, Faculty of Medicine, Universitas Muhammadiyah, Malang, Indonesia**ABSTRACT**

Cats are the host of a wide variety of microorganisms including ectoparasites and endoparasites. One of the endoparasites that infect cats is hookworm. The hookworms consists of two groups, the animal hookworms, and the human hookworms. The manifestation that can be caused by animal hookworms to humans is Cutaneous Larva Migrant (CLM). This study aimed to discover whether hookworm in stray cats (*Felis silvestris catus*) can cause CLM in humans. We performed a systematic search in Pubmed/Medline and Cochrane published between 2016 and 2021 with no restrictions by language, research country, or type of research design. The results of the analysis showed that the high level of hookworms infection in stray cats could increase the risk of CLM in humans. Based on the study, we could conclude that the high prevalence of hookworm infection in cats plays an important role in the increased risk of zoonoses in humans which in turn could also increase the prevalence of CLM in humans.

Keywords: Hookworm; stray cat; cutaneous larva migrant; infectious disease

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Hii j ni j tu

1. Risk factors that can increase the incidence of CLM in humans include male sex, children aged >15 years, low/income people, and daily behaviour of walking outdoors without using footwear, especially on the sand.
2. Risk factors that play the most role in increasing the incidence of CLM in humans are walking outdoors without using footwear, especially on the sand.

INTRODUCTION

Cutaneous Larva Migrant (CLM) is a skin disease caused by filariform larvae of animal hookworms (Baple & Clayton 2015). The prevalence of CLM is very high, especially in developing countries with tropical-subtropical climates (Reichert et al. 2016). The incidence rate of CLM can increase up to fifteen times higher in the rainy season (Leung et al. 2017). The prevalence of hookworm infection in Thailand varies from 0.6% to 13.4%, while in Indonesia, it is 2.4%, 0.6%, 5.1%, 1.6%, and 1.0% from 2002 to 2006 with one of its manifestations is CLM (Kladkempetch et al. 2020).

Stray cats that live freely around human habitations often roaming around dirty places, making them a habitat for various kinds of parasites, one of which is animal hookworm (Taetzsch et al. 2018, Wang et al. 2019). The population of stray cats is also very large and continues to increase. Based on the World Society for the Protection of Animals (WSPA) in 2008, there were 15 million cats in Indonesia, the third-largest in the world (Farantika & Susanti 2019). The large population and the habitats of stray cats close to

humans increase the risk of spreading parasites from cats to humans and causing zoonotic diseases (Jia-Chi et al. 2016). Research conducted by da Silva et al. (2020), that there was a relationship between the presence of animal hookworm eggs in stray cat feces and 59 cases of CLM in humans in Votuporanga, Sao Paulo, Brazil. Besides, the high prevalence of hookworm infection in cats affects the incidence of zoonotic diseases in humans (Pumidonming et al. 2017).

This study aimed to determine whether there is a relationship between the increase in the stray cats population and the physical environment that can support the growth of animal hookworm to the increase in the prevalence of CLM in humans. CLM is a disease that can be diagnosed based on clinical findings. This disease can cause discomfort to patients such as itching and triggering them to tend to scratch. The habit of scratching can lead to secondary skin infections such as cellulitis. In addition, in rare cases, CLM can cause Loeffler syndrome. Therefore, the incidence of CLM can be understood, therapy can be given effectively, and zoonotic infections can be controlled in the future.

MATERIALS AND METHODS

We studied this hypothesis by performing a systematic search of two comprehensive online databases (Pubmed/Medline and Cochrane) using the following keywords: <cutaneous larva migrans> or <creeping eruption> or <CLM> or <HrCLM> AND <stray cat> AND <hookworm>. The diagnosis of CLM was always clinical. Patients were included without considering gender or age. Only literature published between 2016 and 2021 was included to ensure relevance with regard to the current epidemiologic situation. No restrictions by language, research country, or type of research design were applied. Both full-text papers and abstracts were included, as well as case reports and case series were considered. References from selected literature were evaluated, while experts in the field were consulted as additional search sources.

Primary outcomes were prevalence and risk factors for cutaneous larva migrants in humans. Secondary outcomes were prevalence and risk factors of hookworm infection in stray cats that could increase the incidence of CLM in humans. Due to the nature of the data, no meta-analysis or summary measures were calculated.

RESULTS

Several studies show the prevalence rate of stray cats infected by hookworm. The results of a study conducted by Szwabe and Blaszkowska (2017) using the sedimentation technique on a total of 68 fecal samples from stray cats in Poland showed that only 3% of the stool samples studied were positive for hookworm. Another study was conducted by Korkmaz et al. (2016) on 100 fecal samples from stray cats in Kirikkale, Turkey using the flotation technique. The study found that parasites were found in 47% of the total samples, while only 2 samples were positive for hookworm (4.2%). Another study using the flotation technique was also conducted by Fu et al. (2019). In this study, 308 stray cat feces samples were collected from 8 cities in Guangdong Province, China. The results obtained were as many as 47 positive stool samples containing hookworm (15.26%) (Table 1).

The next research discussed the risk factors that affected hookworm infection in cats. The results of research conducted by Wahyudi et al. (2017) using direct smear, sedimentation, flotation, and McMaster techniques on 180 samples of stray cat feces in Surabaya showed that worm eggs were positively

found in 68 samples (37.8%), while hookworm eggs were found in 42 samples (23.3%). Research using a similar technique was conducted by Rabbani et al. (2020) on 120 samples of stray cats and domestic cat feces in Lumajang, East Java, Indonesia. The results of the study showed that 68.33% of cat feces samples contained gastrointestinal parasites, including 18.33% hookworms. A total of 7/60 samples of domestic cat feces and 15/60 samples of stray cat feces contained hookworm. Besides, it was found that 2 domestic cats of <1 year old and 5 domestic cats of >1 year old were infected by hookworm, while 4 stray cats of <1 year old and 11 cats of >1 year old were infected by hookworm.

Another study conducted by Oktaviana et al. (2014) used the flotation technique on 80 samples of a stray cat and domestic cat feces. The results obtained 19/40 samples of stray cat feces (47.5%) and 10/40 samples of domestic cat feces (25%) contained hookworm. Besides, 17/45 male cats (37.8%) and 12/35 female cats (34.3%) were infected by hookworm. The results of research conducted by Fu et al. (2019) showed that of the 47 stray cats, 8/47 aged <1 year (17.02%) and 7/47 >1 year (14.89%) were positively infected by hookworm, while 19.14% of male cats and 12.76% of female cats were positively infected by hookworm (Table 2).

Subsequent research also discussed the risk factors that most affected hookworm infection in cats. The results of research conducted by Rabbani et al. (2020) using a cross-sectional study method showed that the physical environment which includes soil texture, temperature, humidity, hygiene, and sanitation are risk factors that could affect the level of hookworm infection in cats. Based on the statistical analysis of the study, it obtained the following data, where sandy soil texture had an infection prevalence of 33.1% with a p-value of 0.764, wet soil had an infection prevalence of 47.7% with a p-value of 0.028, a temperature of more than 28.6-29.5C has an infection prevalence of 55.8% with a p-value=0.000, a humidity of 66% has an infection prevalence of 55.8% with a p-value=0.000, and poor water sanitation has an infection prevalence of 43.8% with p-value=0.000. A similar study was conducted by Fu et al. (2019) found that sandy soil texture has an infection prevalence of 47.2% with a p-value of 0.537, the temperature has an infection prevalence of 61.1% with a p-value of 0.000, and humidity has an infection prevalence of 61.1% with p-value=0.000 (Table 3).

Table 1. Prevalence of stray cats infected by hookworm

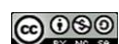
Lists of study	Method	Sample	Result
Szwabe and Blaszkowska (2017)	Sedimentation technique	68 fecal samples from stray cats in Poland	As many as 3% of the total samples were detected positive for hookworm
Korkmaz et al. (2016)	Flotation technique	100 fecal samples from stray cats in Kirikkale, Turkey	As many as 47% of all samples were found to be parasitic, only 2 samples were positive for hookworm (4.2%)
Yeqi Fu et al. (2019)	Flotation technique	308 stray cat feces samples from 8 cities in Guangdong, Province, China	A total of 47 stool samples were positive for hookworm (15.26%)

Table 2. Risk factors that affected hookworm infection in cats

Lists of study	Method	Sample	Result
Wahyudi et al. (2017)	Direct smear, sedimentation, flotation, and McMaster	180 samples of stray cat feces in Surabaya	42 samples (23.3%) were positive for hookworm eggs
Rabbani et al. (2020)	Direct smear, sedimentation, flotation, and McMaster	120 samples of a stray cat and domestic cat feces in Lumajang	Cat infected by hookworm
			Domestic cat (n=60) Stray cat (n=60)
			<ul style="list-style-type: none"> • 15 (25%) Number of cat • 7 (11.6%) Age (years old) • <1 y.o: 4 (26.66%) • <1 y.o: 2 (28.57%) • >1 y.o: 5 (71.42%) • >1 y.o: 11 (73.33%)
Oktaviana et al. (2014)	Flotation	80 samples of a stray cat and domestic cat feces in Denpasar	Cat infected by hookworm
			Domestic cat (n=40) Stray cat (n=40)
			Female (n=35) Male (n=45)
			<ul style="list-style-type: none"> 10 (25%) 19 (47.5%) 12 (34.3%) 17 (37.8%)
Yeqi Fu et al. (2019)	Flotation	47 stray cats	Cat infected by hookworm
			<ul style="list-style-type: none"> Age • <1 year : 8 (17.02%) • >1 year : 7 (14.89%) Gender • Female: 12.76% • Male: 19.14%

Table 3. Risk factors that most affected hookworm infection in cats

Lists of study	Variable	Prevalence of infection	p-value
Rabbani et al. (2020)	Sandy soil	33.1%	0.764
	Wet soil	47.7%	0.028
	Temperature >28.6-29.5C	55.8%	0.000
	Humidity 66%	55.8%	0.000
	Poor water sanitation	43.8%	0.000
Yeqi Fu et al. (2019)	Sandy clay loam	47.2%	0.537
	Temperature	61.1%	0.000
	Humidity	61.1%	0.000



Further studies discussed the prevalence of CLM in humans in several countries. The results of research by Sow et al. (2017) using a retrospective study method showed that the prevalence of CLM in France was 1-3% found in people who recently returned from endemic countries. The case study conducted by Guidice et al. (2019) found that there were 5 cases of autochthonous CLM (patients with no history of travel to tropical countries or CLM that occurred in the local area) in France in the last 25 years. Another study conducted by Reichert et al. in 2016, that the prevalence of CLM in Brazil was around 0.2% to 4.4-14.9% of the total general population, in the dry season and rainy season, respectively.

Subsequent studies discussed the risk factors that increased the incidence of CLM in humans, including gender, age, economic conditions, daily behavior, and environmental conditions. The research results of Reichert et al. (2016) in Manaus, Brazil showed that the number of CLM infections found in humans was caused by several factors, such as gender, including 44 males (13.4%) and 22 females (4.6%) cases. Based on age groups, it consisted of <4 years, 5-9 years, 10-14 years, 15-19 years, and >20 years with 15 (8.6%), 23 (14.4%), 16 (18.2%), 1 (2.2%), and 11 (3.3%) cases respectively. The economic conditions of the subject included poor, intermediate, and rich with 37 (11.5%), 21 (8%), and 8 (4%) cases respectively.

Other factors such as daily behavior (i.e., walking on the ground barefoot, wearing footwear, walking on the sandy ground with no footwear, frequently wearing footwear, and always wearing footwear with 14/58 (24.1%), 52/731 (7.1%), 29/111 (26.1%), 33/420 (7.9%), and 4/269 (1.5%), respectively. In the case of environmental conditions which included whether or not the soil was contaminated with cat feces, found that as many as 17/103 cases (16.5%) were in an environment, where cat feces were present and 49/702 cases (7%) were found in an environment with no cat feces.

The results of another study conducted by Reichert et al. (2016) show data on the incidence of CLM per year on several factors such as gender, including male (0.86) and female (0.25); regarding the economic conditions of the people, including poor (0.68), intermediate (0.47), and rich (0.31); regarding daily behavior such as walking on the ground barefoot (0.78) and wearing footwear (0.48), walking on the sandy

ground by never wearing footwear (0.90), often wearing footwear (0.49), and always wearing footwear (0.29). Another study conducted by Sow et al. (2017) obtained data on the number of CLM infections in humans toward several factors such as gender, including 22 cases (51.2%) in males and 21 cases (48.8%) in females; based on age, namely aged <25 years, 25-50 years old, and >50 years old with 9 (20.9%), 29 (67.5%), and 5 (11.6%) cases respectively. Similar research was also conducted by Heryantoro (2011) in Kulon Progo, Indonesia, that obtained data on the number of CLM infections in humans toward several factors such as gender, there are 54 cases (67.5%) in male and 26 cases (32.5%) in female; based on age, namely aged <15 and >15 years old with 46 (57.5%), and 34 (42.5%) cases, respectively (See Table 4).

Another research discussed the risk factors that most affected increasing the incidence of CLM in humans which included gender, age, economic conditions, daily behavior, and environmental conditions. The results of statistical analysis from the research of Reichert et al. (2016) were as follows: gender included male (OR = 3.21) and female (OR = 1); age <4 years (OR = 2.80), 5-9 years old (OR = 4.99), 10-14 years old (OR = 6.61), 15-19 years old (OR = 0.66), and >20 years old (OR = 1); the economic condition of the people which includes poor (OR = 3.16), intermediate (OR = 2.10), and rich (OR = 1); daily behavior such as walking on the ground barefoot (OR = 4.16), wearing footwear (OR = 1), walking on the sand with never wearing footwear (OR = 23.43), often wearing footwear (OR = 5.65), and always wearing footwear (OR = 1); the environmental condition which includes whether or not the soil was contaminated with cat feces, the environment that did contained cat feces (OR = 2.63), and the environment that did not contain cat feces (OR = 1). A similar study was conducted by Reichert et al. (2016) where the data obtained from statistical analysis based on the percentage of CLM incidence of each individual per year are as follows, gender includes male (0.86) and female (0.25); age <4 years (0.38), 5-9 years (0.46), 10-14 years (0.93), and 15-18 years (0.26); The economic condition of the people which includes the poor (0.68), intermediate (0.47) and rich (0.31); daily behavior such as walking on the ground barefoot (0.78), with wearing footwear (0.48), walking on sand with never wearing footwear (0.90), often wearing footwear (0.49), and always wearing footwear (0.29) (Table 4).

Table 4. Risk factors that increased the incidence of CLM in humans

	Variable	CLM (%)	OR (CI 95%)	p-value		
Reichert et al. (2016)	Gender	Male	44 (13.4)	3.21	<0.001	
		Female	22 (4.6)	1		
	Age	≤ 4 years old	15 (8.6)	2.80	0.012	
		5-9 years old	23 (14.4)	4.99	<0.001	
		10-14 years old	16 (18.2)	6.61	<0.001	
		15-19 years old	1 (2.2)	0.66	0.695	
		≥ 20 years old	11 (3.3)	1		
	Economic condition	Poor	37 (11.5)	3.16	0.004	
		Intermediate	21 (8.0)	2.10	0.081	
		Rich	8 (4.0)	1		
	Daily behavior	Walking on the ground				
		Barefoot	14/58 (24.1)	4.16	<0.001	
		With wearing footwear	52/731 (7.1)	1		
		Walking on the sandy ground				
Never wearing footwear		29/111 (26.1)	23.43	<0.001		
Often wearing footwear		33/420 (7.9)	5.65	0.001		
Environmental condition	Always wearing footwear	4/269 (1.5)	1			
	Animal feces on compound	17/103 (16.5)	2.63	0.001		
	No animal feces on compound	49/702 (7.0)	1			
	Gender	Male	57	0.86	3.41	<0.001
Female		21	0.25	1		
Reichert et al. (2018)	Economic condition	Poor	41	0.68	2.15	0.024
		Intermediate	23	0.47	1.51	0.259
	Rich	11	0.31	1		
Daily behavior	Walking on the ground					
	Barefoot	14	0.78	1.57	0.126	
	With wearing footwear	64	0.48	1		
	Walking on the sandy ground					
	Never wearing footwear	25	0.90	3.24	0.002	
	Often wearing footwear	44	0.49	1.66	0.168	
	Always wearing footwear	9	0.29	1		
Sow et al. (2017)	Variable			CLM (%)		
		Gender	Male	22 cases (51.2)		
		Female	21 cases (48.8)			
	Age	<25 years old	9 (20.9)			
25-50 years old		29 (67.5)				
>50 years old		5 (11.6)				
Heryantoro et al. (2012)	Gender	Male	54 cases (67.5)			
		Female	26 cases (32.5)			
Age	<15 years old	46 (57.5)				
	>15 years old	34 (42.5)				

DISCUSSION

Prevalence of stray cats infected by hookworm

Regional conditions (climate, humidity, temperature and soil conditions) are important things that may affect prevalence rates. State that geographical factors of a region can affect prevalence rates, other factors including climate (Abu-Madi et al. 2008). The difference in the prevalence of hookworm infection in cats obtained from Poland (3%) (Szwabe & Blaszkowska 2017) and Turkey (4.2%) (Korkmaz et al.

2016) compared to China (15.26%) (Fu et al. 2019) was quite far (See Table 1). This is because Poland and Turkey are not tropical countries, while Guangdong Province, China, is an area with a tropical climate. Based on these three studies, the climatic conditions of an area affect the prevalence of hookworm infection in cats. The tropical climate has high humidity so that it is a fertile ground for the life of parasitic worms. Tropical climates have a higher prevalence of hookworm infection in cats than in non-tropical areas. This is because high humidity is an optimum condition for the development and dissemination of various species of



worm diseases and areas with tropical climates tend to have warm temperatures between 23-30°C, humidity levels of 80-100%, and the existence of a long rainy season that can maintain the scale of infection in endemic proportions, support larval growth, and help infective larvae to survive on the ground. In other conditions, lower temperatures making egg development takes longer or inhibits egg's hatch (Farantika, R et al. 2019; Sucitrayani et al., 2014)..

Risk factors that affected hookworm infection in cats

Another factor that made of the high prevalence of worm infections in stray cats is because most cats forage in trash cans. Stray cats live in moist and dirty areas where these environments are ideal conditions for the development of an infective form of worm larvae (Oktaviana et al., 2014). Based on the previous four studies (Table 2), it is known that stray cats are more at risk for hookworm infection than domestic cats, because stray cats live untreated, consume food that is not nutritious, and live in a dirty, humid, and poor sanitation environment that are ideal conditions for the development of infective larvae of hookworms. The prevalence of hookworm infection in cats aged <1 year and >1 year did not have a significant difference, as well as the prevalence of hookworm infection in male and female cats. We briefly reported that the most important factor influencing the level of hookworm infection in cats is the physical environmental conditions which include hygiene, temperature, humidity, and sanitation, with the risk factors that most affect the level of hookworm infection in cats (i.e., temperature and humidity with a p-value of 0.000) (Table 3).

Prevalence and risk factors of CLM in humans

The data on CLM prevalence in humans obtained from each region may vary because there are several factors that influence it, especially climate. The prevalence of CLM in humans in Brazil was higher than in France because Brazil is a country with a tropical climate, while France does not have a tropical climate. In tropical countries, the prevalence of CLM in animals and humans tends to be high. The high prevalence of hookworm infection in cats plays an important role in increasing the risk of zoonoses in humans which can increase the prevalence of CLM in humans (Pumidonming et al. 2017).

Based on the previous four studies, males were more at risk of developing CLM than females, because they were more likely to have contact with the ground than

females. Research conducted by Reichert et al. (2016) stated that the age most at risk for CLM was children or individuals aged <15 years, because they tend to play outdoors without wearing footwear, resulting in direct contact between the skin and the ground or sand. Different statements were obtained from a study that the age most at risk for CLM is individuals aged 25-50 years (Sow et al. 2017). This difference can occur because the research was conducted in France, which was not a CLM endemic country, so the collected data comes from people who have traveled or have just returned from a CLM endemic country.

Another factor that can increase the risk of getting CLM is economic conditions. In this case, the poor tend to be at risk for CLM, because people with low economy usually live simple and are limited life. People with low economy tend to live in dirty and slum environments and consume less nutritious food, so they are vulnerable to getting CLM. Another influential factor in increasing the risk of developing CLM is walking outdoors (i.e., on the sandy ground) with no shoes. Sandy soil is one of the physical environmental factors that support the development of hookworm larvae. Walking outside barefoot will increase direct contact between sand or soil with the skin, which then allows infective larvae to penetrate directly into the skin, causing the CLM. It can be concluded that the most influential risk factor in increasing the incidence of CLM in humans is daily behavior, such as walking on the sand barefoot.

Our study can answer the question of why developing countries with tropical climates have a higher prevalence of CLM than non-tropical countries. Based on the results of the study, we can determine the risk factors that play the most role in causing hookworm infection in stray cats, zoonotic infections, and the incidence of CLM in humans. Tropical countries have a higher prevalence of hookworm infection in cats and humans than non-tropical countries; physical environmental conditions that include hygiene, temperature, humidity, and sanitation affect the rate of hookworm infection in cats and humans; the high prevalence of hookworm infection in cats plays an important role in increasing zoonotic infections in humans which then can increase the prevalence of CLM in humans. Developing countries with tropical to subtropical climates have a physical environment (temperature and humidity) that supports the growth of animal hookworm larvae. In addition, the management and control of the stray cat population are also not good. Environmental hygiene and water sanitation in some places in developing countries are also poor. That was the cause of the high prevalence of CLM in

developing countries, especially those with tropical-subtropical climates.

Strength and limitation

In this study, we found that there were not many studies that discussed hookworm and CLM. There were also little data on the prevalence of CLM, especially in Indonesia. Many researchers had discussed the number of hookworm eggs in cat or dog feces, but only a few had associated it with the prevalence of CLM. Therefore, the further research study is suggested to discuss the relationship between the animal hookworm eggs in stray cat feces and the incidence of CLM in an area.

CONCLUSION

Hookworm in stray cats (*Felis silvestris catus*) can cause CLM in humans. The high prevalence of hookworm infection in cats plays an important role in the increased risk of zoonoses in humans which in turn can increase the prevalence of CLM in humans. In addition, tropical climate, sandy soil, and physical environmental conditions including temperature, humidity, hygiene, and sanitation affect the level of hookworm infection in cats and humans.

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Conflict of interest

None0

Funding disclosure

Pone0

Author contribution

FIM, S, and RKP contributed in the conception of the study idea, data collection and analysis, revise the manuscript. S was final approval to be published and agreement to be accountable for all aspects.

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