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Systematic Review

The Global Prevalence of *Diphyllobothrium* in Dogs, and Cats: A Systematic Review and Meta-analysis

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ABSTRACT

Background: Fish tapeworms of the genus *Diphyllobothrium* are pseudophyllidean cestodes transmitted through the consumption of raw or inadequately cooked fish.

Objective: The current systematic review and meta-analysis aim to estimate the global prevalence of *Diphyllobothrium* in dogs and cats based on published literature.

Methods: Multiple English databases (PubMed, Scopus, ProQuest, Web of Science, and Google Scholar) were explored for relevant papers published until December 2021.

Findings: Among the 37 studies that were included, 32 documented *Diphyllobothrium* infection in dogs and five in cats. The pooled prevalence (95% confidence interval) was 0.060% (0.030%-0.100%). The analysis based on country showed that the highest pooled prevalence in dogs and cats was observed in Bangladesh (0.250%, 0.149%-0.366%) and Indonesia (0.254%, 0.182%-0.333%), respectively. Based on the continent, Africa (0.109%, 0.017%-0.264%) and Asia (0.060%, 0%-0.345%) were the most common regions for infection in dogs and cats, respectively. Among different diagnostic methods, the highest pooled prevalence was related to molecular (0.661%, 0.573%-0.743%) and parasitological techniques (0.041%, 0%-0.217%) for dogs and cats' studies, respectively.

Conclusion: The findings show the importance of establishing a prevention and control measure focused on improving regular deworming and enhancing awareness of parasitic zoonotic diseases to minimize the transmission risk.

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1. Introduction

Diphyllobothrium latum (Linnaeus 1785), also known as fish tapeworm or broad tapeworm, is a globally distributed member of the Pseudophyllidea order [1, 2]. *Diphyllobothrium* has 15 species that infect humans, and it is estimated that more than twenty million people in the world are affected by different species of the parasite. The most frequent causative agents in humans are known as *D. latum* and *D. nihonkaiense* [3, 4].

The three-host life cycle of *D. latum* includes copepods of the genera *Arctodiaptomus*, Cyclops, *Diaptomus*, *Ectocyclops*, Hemidiaptoms, and Mesocyclops serve as the first intermediate hosts, while freshwater and native fishes, mainly several species of pike, perch, salmon, trout, grayling, barbel, and burbot, are the second intermediate hosts [5-7]. It inhabits the small intestine of fish-eating mammals (definitive hosts), including dogs, cats, foxes, pigs, and other piscivorous animals, as well as humans (accidental hosts) [8-10].

The mature parasites lay 1 million eggs daily. The eggs develop into coracidium in 10 days if they reach an aquatic environment where they may be ingested by copepods. Within 14-21 days, coracidium develops into procercoid larvae in the body cavity of the copepod host. After the infected copepods are ingested by the fish, the procercoid larvae have the opportunity to penetrate the intestinal wall, where they develop into plerocercoid larvae in the muscle tissues. If the infected fish is ingested by definitive and accidental hosts, the plerocercoid larvae develop into adults within 21-35 days [7, 9].

Diphyllobothriasis is a zoonotic fish-borne disease mostly caused by *D. latum*. Recently, the re-emergence of the disease is reported in several regions of the world, which may be due to alterations in eating habits, rapid freezing procedures, and globalization [2]. Humans acquire it through the consumption of raw or undercooked infected fish [11]. Infection in dogs and cats occurs via eating raw fish, discarded viscera, and feeding fish waste to them [12].

The disease causes pernicious anaemia and cognitive decline as a result of vitamin B12 deficiency in definitive hosts [2, 13]. Furthermore, ocular, gastrointestinal, respiratory, central nervous system and dermatological manifestations are reported [2]. A single dose of praziquantel (7.5 mg/kg) is an effective treatment for *Diphyllobothrium* infection in dogs and cats [14].

The current systematic review and meta-analysis aimed to estimate the global prevalence of *Diphyllobothrium* infection in dogs and cats. This information is essential to understand the circulation of these parasites in the natural environment, to investigate the endemic regions, and to consider preventive measures to reduce the incidence of the infection in definitive hosts. Furthermore, evaluating the infection rate in dogs and cats on a global scale can help assess the potential risk factors for humans, as these parasites have zoonotic features.

2. Materials and Methods

Search strategy

This study was elaborated according to the preferred reporting items for systematic reviews and meta-analysis checklist (PRISMA) [15]. A search was conducted in multiple databases, including Scopus, PubMed, ProQuest, Web of Science, and Google Scholar. Additionally, a hand search was conducted for the bibliographies published until December 2021. Search terms related to *Diphyllobothrium*, *Diphyllobothrium spp*., *Diphyllobothrium latum*, Diphyllobothriasis, fish tapeworm, foodborne diseases, foodborne parasites, intestinal helminths, dogs, cats, prevalence, frequency, global, worldwide using AND and or OR Boolean operators. The duplicates and irrelevant papers were removed, and the reference lists of obtained articles were screened for further studies that were not found through a database search. Two independent authors performed the search process, evaluated titles and abstracts, and reviewed the full texts.

Inclusion and exclusion criteria

Full-text literature was evaluated for eligibility if they met the inclusion criteria, including cross-sectional studies reporting the prevalence of *Diphyllobothrium* in dogs and cats, peer-reviewed original papers, having accessible full-text and abstract in English, having a total sample size and an exact number of positive cases, and articles published in English until December 2021. Case reports, case series, review articles, publications with non-original data, letters, editorials, and papers with unclear or undetermined results, as well as papers written in other languages, were excluded. Moreover, those articles that reported *Diphyllobothrium* infection in humans and in animals other than dogs and cats were excluded from the analyses of the current study. A Microsoft Excel® version 2016 was used to separately collect the following information, which was retrieved from each of the included articles, first author's name, publication year, the country where the study was conducted, continent, sample size, number of positive samples, types of animals, human development index (HDI), climate, average temperature, annual rainfall, humidity, *Diphyllobothrium Spp/. Diphyllobothrium latum* and diagnostic methods including morphological detection and molecular techniques (Tables 1, 2 and 3).

Quality assessment

A Newcastle-Ottawa Scale was implemented to assess the quality of included studies (Supplementary Table 1) [16]. Scoring was based on the following three items, selection (maximum of 5 stars), comparability (maximum of 2 stars), and outcome (maximum of 3 stars) [17-20].

Data synthesis and statistical analysis

The pooled prevalence of *Diphyllobothrium* in dogs and cats reported globally was calculated with a 95% confidence interval. Egger test and Begg's test were applied to specify the possible publication bias. Moreover, publication bias was assessed by the Luis Furuya-Kanamori (LFK) index, and Doi plot [21]. An LFK index within the range of ±1, ±2, and outside ±2 is considered symmetrical (no publication bias), slightly/minor asymmetric, and significantly/major asymmetric, respectively.

A Freeman-Tukey double arcsine transformation of the random-effects model was used to compute the pooled prevalence estimates. Cochrane's Q test and inconsistency index (I^2 statistics) were used to assess the magnitude of heterogeneity among included studies, with I^2 values of 25%, 50%, and 75% considered low, medium, and high heterogeneity, respectively. A P value less than 0.05 was set as statistically significant. All statistical analyses were conducted using the meta-package of R (version 3.6.1) [22].

3. Results

Search results and study selection

The initial database search identified 973 articles, including 41 from PubMed, 58 from Scopus, 46 from ProQuest, 39 from Web of Science, and 789 from Google Scholar. Of the 758 records screened, 612 articles were excluded because they did not meet the inclusion criteria. Of the 146 full-text articles assessed for eligibility, 109 articles were excluded for the following reasons; 9 papers without sufficient data, 7 multiple studies with overlapping data, 48 case reports or case series, and 45 studies with no original data, including reviews, letters, theses, or workshops. Among 37 studies included in the current systematic review and meta-analysis, 32 studies reported *Diphyllobothrium* infection in dogs, and 5 studies reported in cats (Figure 1).

The overall pooled prevalence of *Diphyllobothrium* infection in dogs and cats was 0.060% (95% CI: 0.030%-0.100%) (Figure 2).

For dog hosts, a total of 32 studies (16,541 cases) were analysed, of which 696 harboured *Diphyllobothrium* parasites (Table 2). The global pooled prevalence rate for dogs was 0.064% (95% CI, 0.030%-0.109%) (Figure 2). According to the species of the parasite, the estimated pooled prevalence was as follows, 0.065% (95%CI, 0.014%-0.151%) for *D. latum*, and 0.062% (95%CI, 0.024%-0.117%) for *Diphyllobothrium* spp. (Table 2). The highest prevalence was found in the continent of Africa (0.109%, 95% CI, 0.017%-0.264%), and regarding countries, our analysis showed that Bangladesh had the highest pooled prevalence (0.250%, 95% CI=0.149%-0.366%) (Table 2). The analysis based on different climates and climatic parameters showed that the infection was most prevalent in regions with a tropical savannah climate (0.101%, 95% CI, 0.025%-0.200%), the average temperature of > 20°C (0.096%, 95% CI, 0.020%-0.220%), annual rainfall of > 1500 mm (0.109%, 95% CI, 0.019%-0.259%), and humidity of 40-75 (0.081%, 95% CI, 0.037%-0.140%). The pooled prevalence rate concerning the HDI was the highest for low-level countries (0.117%, 95% CI, 0.007%-0.332%) (Table 2). The estimation of pooled prevalence based on the diagnostic method showed that the highest pooled prevalence was related to molecular technique with one study (0.661%, 95% CI, 0.573%-0.743%).

For cat hosts, a total of 5 studies (1,512 cases) were analysed, of which 39 harboured *Diphyllobothrium* infection (Table 3). The global pooled prevalence rate for cats was 0.041% (95% CI, 0%-0.217%) (Figure 2). According to the parasite species, the estimated pooled prevalence was as follows; 0.059% (95% CI, 0%-0.346%) for *Diphyllobothrium latum*, and 0.002% (95% CI, 0%-0.008%) for *Diphyllobothrium spp*. (Table 3). The highest prevalence was related to the continent of Asia (0.060%, 95% CI, 0%-0.345%), and we found that Indonesia had the highest pooled prevalence (0.254%, 95% CI=0.182%-0.333%) among different countries (Table 3). The analysis based on different climates and climatic parameters showed that the infection was most prevalent

Table 1. Main characteristics of the included studies reporting the prevalence of *Diphyllobothrium* in dogs and cats

Study No.	Authors	Country	Continent	Types of Animals	*Diphyllobothrium Spp./ Diphyllobothrium latum*
1	Unruh et al. 1973 [44]	Canada	North America	Dogs	*Diphyllobothrium* spp.
2	Torres et al. 1989 [45]	Chile	South America	Dogs	*Diphyllobothrium* spp.
3	Arenas et al. 1991 [46]	Chile	South America	Dogs	*Diphyllobothrium* spp.
4	Zunino et al. 2000 [47]	Argentina	South America	Dogs	*Diphyllobothrium* spp.
5	Barutzki and Schaper 2003 [48]	Germany	Europe	Dogs	*Diphyllobothrium latum*
6	Milano and Oscherov 2005 [49]	Argentina	South America	Dogs	*Diphyllobothrium* spp.
7	Sager et al. 2006 [50]	Switzerland	Europe	Dogs	*Diphyllobothrium latum*
8	Pullola et al. 2006 [51]	Finland	Europe	Dogs	*Diphyllobothrium latum*
9	Dai et al. 2009 [52]	China	Asia	Dogs	*Diphyllobothrium latum*
10	Umar 2009 [53]	Nigeria	Africa	Dogs	*Diphyllobothrium latum*
11	Soriano et al. 2010 [54]	Argentina	South America	Dogs	*Diphyllobothrium latum*
12	Bajalan et al. 2010 [55]	Iraq	Asia	Dogs	*Diphyllobothrium latum*
13	Nwoha and Ekwuruike 2010 [56]	Nigeria	Africa	Dogs	*Diphyllobothrium latum*
14	Mocetti et al. 2011 [57]	Peru	South America	Dogs	*Diphyllobothrium* spp.
15	Schurer et al. 2012 [58]	Canada	North America	Dogs	*Diphyllobothrium* spp.
16	Al-Obaidi et al. 2012 [59]	Iraq	Asia	Dogs	*Diphyllobothrium* spp.
17	Santos et al. 2012 [60]	Brazil	South America	Dogs	*Diphyllobothrium* spp.
18	Das et al. 2012 [61]	Bangladesh	Asia	Dogs	*Diphyllobothrium latum*
19	Abere et al. 2013 [62]	Ethiopia	Africa	Dogs	*Diphyllobothrium latum*
20	Islam et al. 2014 [63]	India	Asia	Dogs	*Diphyllobothrium latum*
21	Schurer et al. 2014 [64]	Canada	North America	Dogs	*Diphyllobothrium* spp.
22	Semenas et al. 2014 [37]	Argentina	South America	Dogs	*Diphyllobothrium* spp.
23	Rivero et al. 2015 [1]	Argentina	South America	Dogs	*Diphyllobothrium* spp.
24	Amissah-Reynolds et al. 2016 [23]	Ghana	Africa	Dogs	*Diphyllobothrium latum*
25	Yadav and Shrestha 2017 [65]	Nepal	Asia	Dogs	*Diphyllobothrium* spp.
26	Flores et al. 2017 [66]	Argentina	South America	Dogs	*Diphyllobothrium* spp.
27	Roth et al. 2018 [5]	Argentina	South America	Dogs	*Diphyllobothrium latum*
28	Little et al. 2019 [67]	USA	North America	Dogs	*Diphyllobothrium latum*
29	Suganya et al. 2019 [68]	India	Asia	Dogs	*Diphyllobothrium latum*
30	Gebremedhin et al. 2020 [69]	Ethiopia	Africa	Dogs	*Diphyllobothrium* spp.
31	Cisneros et al. 2020 [70]	Peru	South America	Dogs	*Diphyllobothrium* spp.
32	Ikejiofor et al. 2021 [71]	Nigeria	Africa	Dogs	*Diphyllobothrium latum*
33	Sohn et al. 2005 [72]	South Korea	Asia	Cats	*Diphyllobothrium* spp.
34	Al-Rubaie et al. 2015 [73]	Iraq	Asia	Cats	*Diphyllobothrium latum*
35	Yudhana et al. 2017 [74]	Indonesia	Asia	Cats	*Diphyllobothrium latum*
36	Zottler et al. 2019 [75]	Switzerland	Europe	Cats	*Diphyllobothrium latum*
37	Barua et al. 2020 [76]	Bangladesh	Asia	Cats	*Diphyllobothrium latum*

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Table 2. Sub-group analysis based on HDI, continent, detection method, climate, countries, average temperature, humidity, and annual rainfall and *Diphyllobothrium Spp./Diphyllobothrium latum* in included studies in dogs

Variables		No. Studies	Sample Size	Infected	Pooled Prevalence (95% CI)	Heterogeneity		
						I^2	τ^2	P
Dog								
HDI	Very high	16	13 697	517	0.070 (0.015-0.159)	99	0.069	<0.001
	High	4	715	8	0.011 (0.006-0.017)	0	0	0.91
	Medium	7	1 253	49	0.058 (0.010-0.143)	91	0.020	<0.001
	Low	5	876	122	0.117 (0.007-0.332)	97	0.043	<0.001
	Total	32	16 541	696	0.064 (0.030-0.109)	98	0.047	<0.001
Continent	Africa	6	1 030	133	0.109 (0.017-0.264)	97	0.035	<0.001
	Asia	7	1 537	43	0.047 (0.004-0.130)	90	0.023	<0.001
	Europe	3	9 484	13	0.001 (0-0.0.385)	37	0	0.20
	North America	4	2 646	345	0.060 (0-0.0.385)	99	0.069	<0.001
	South America	12	1 844	162	0.083 (0.014-0.199)	97	0.069	<0.001
	Total	32	16 541	696	0.064 (0.030-0.109)	98	0.047	<0.001
Detection method	Molecular technique	1	118	78	0.661 (0.573-0.743)	-	-	-
	Parasitology examination	31	16 423	618	0.053 (0.026-0.088)	98	0.032	<0.001
	Total	32	16 541	696	0.064 (0.030-0.109)	98	0.047	<0.001
Climate	Arid climate	2	105	8	0.063 (0-1.000)	80	0.017	0.02
	Humid continental	3	1 444	344	0.094 (0-0.699)	99	0.071	<0.001
	Humid subtropical climate	10	3 336	140	0.075 (0.004-0.220)	98	0.084	<0.001
	Oceanic climate	4	9 214	48	0.037 (0-0.228)	97	0.035	<0.001
	Subarctic climate	1	541	2	0.003 (0-0.10)	-	-	-
	Tropical rainforest climate	3	277	3	0.008 (0-0.28)	0	0	0.85
	Tropical savanna climate	9	1 624	151	0.101(0.025-0.200)	97	0.036	<0.001
	Total	32	16 541	696	0.064 (0.030-0.109)	98	0.047	<0.001
Countries	Argentina	7	1 296	122	0.120 (0.002-0.374)	98	0.103	<0.001
	Bangladesh	1	60	15	0.250 (0.149-0.366)	-	-	-
	Brazil	1	45	1	0.022 (0-0.084)	-	-	-
	Canada	3	1 444	344	0.101 (0-0.699)	99	0.071	<0.001
	Chile	2	271	37	0.115 (0-1.000)	90	0.018	<0.001
	China	1	438	5	0.011 (0.003-0.023)	-	-	-
	Ethiopia	2	356	9	0.045 (0-1.000)	87	0.019	<0.001
	Finland	1	541	2	0.003(0-0.010)	-	-	-
	Germany	1	8 438	9	0.001 (0-0.001)	-	-	-
	Ghana	1	154	11	0.071 (0.036-0.117)	-	-	-
	India	2	534	3	0.010 (0-0.611)	46	0.004	<0.001
	Iraq	2	105	8	0.063 (0-1.000)	81	0.017	<0.001
	Nepal	1	400	12	0.030 (0.015-0.048)	-	-	-
	Nigeria	3	520	113	0.177 (0-0.701)	97	0.048	<0.001
	Peru	2	232	2	0.008 (0-0.028)	0	0	85
	Switzerland	1	505	2	0.004(0-0.011)	-	-	-
	USA	1	1 202	1	0.0008(0-0.003)	-	-	-
	Total	32	16 541	696	0.064 (0.030-0.109)	98	0.047	<0.001

	Variables	No. Studies	Sample Size	Infected	Pooled Prevalence (95% CI)	Heterogeneity		
						I^2	τ^2	P
Average temperature (°C)	<10	4	1 985	346	0.064 (0-0.380)	99	0.064	<0.001
	10-20	20	13 243	207	0.053 (0.015-0.111)	97	0.050	<0.001
	> 20	8	1 313	143	0.096 (0.020-0.220)	97	0.039	<0.001
	Total	32	16 541	696	0.064 (0.030-0.109)	98	0.047	<0.001
Humidity	40-75	26	7 131	671	0.081 (0.037-0.140)	98	0.051	<0.001
	>75	6	9 410	25	0.012 (0-0.040)	87	0.006	<0.001
	Total	32	16 541	696	0.064 (0.030-0.109)	98	0.047	<0.001
Annual rainfall	<400	4	337	10	0.027 (0-0.131)	77	0.012	<0.001
	401-1000	8	10 848	403	0.062 (0.006-0.167)	99	0.039	<0.001
	1001-1500	13	3 982	141	0.057 (0.006-0.154)	97	0.068	<0.001
	>1500	7	1 374	142	0.109 (0.019-0.259)	97	0.042	<0.001
	Total	32	16 541	696	0.064 (0.030-0.109)	98	0.039	<0.001
Diphyllobothrium Spp./ Diphyllobothrium latum	*Diphyllobothrium spp.*	16	3 699	449	0.062 (0.024-0.117)	97	0.030	<0.001
	Diphyllobothrium latum	16	12 842	247	0.065 (0.014-0.151)	98	0.067	<0.001
	Total	32	16 541	696	0.064 (0.030-0.109)	98	0.047	<0.001

HDI: Human development index.

PRISMA: preferred reporting items for systematic reviews and meta-analysis checklist; HDI: human development index; LFK: Luis Furuya-Kanamori; ITS: internal transcribed spacer.

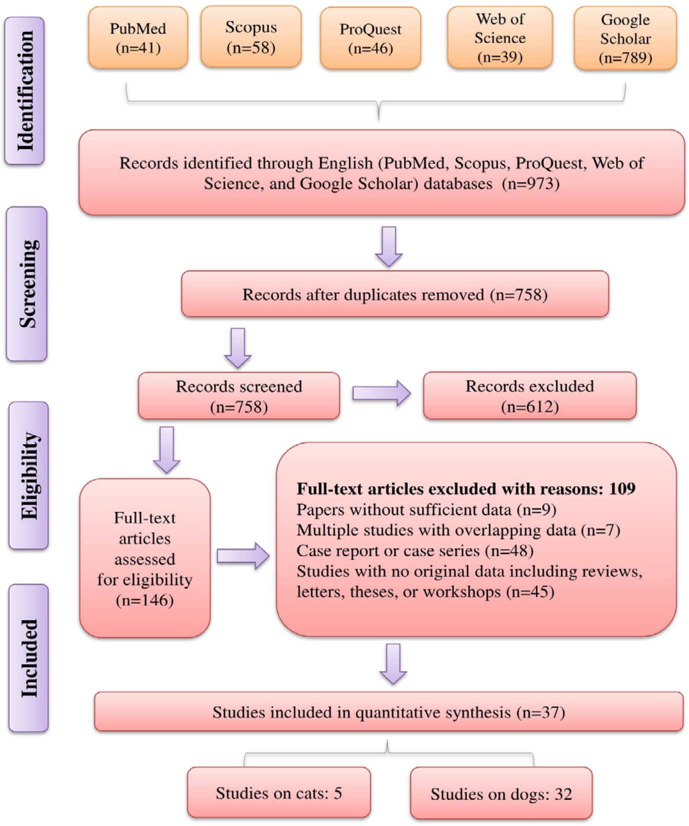

Figure 1. Flow diagram of the study design process

Table 3. Sub-group analysis based on HDI, continent, detection method, climate, countries, average temperature, humidity, and annual rainfall and *Diphyllobothrium Spp./ Diphyllobothrium latum* in included studies in cats

Variables		No. Studies	Sample Size	Infected	Pooled Prevalence (95% CI)	Heterogeneity		
						I^2	τ^2	P
Cat								
HDI	High	3	1228	34	0.040 (0-0.609)	98	0.076	<0.001
	Medium	1	254	1	0.003 (0-0.015)	-	-	-
	Low	1	30	4	0.133(0.037-0.275)	-	-	-
	Total	5	1512	39	0.041 (0-0.217)	96	0.048	<0.001
Continent	Asia	4	848	38	0.060 (0-0.345)	97	0.053	<0.001
	Europe	1	664	1	0.001 (0-0.0.005)	-	-	-
	Total	5	1512	39	0.041 (0-0.217)	96	0.048	<0.001
Detection method	Parasitology examination	5	1512	39	0.041 (0-0.217)	96	0.048	<0.001
	Total	5	1512	39	0.041 (0-0.217)	96	0.048	<0.001
Climate	Arid climate	1	254	1	0.003 (0-0.015)	-	-	-
	Humid subtropical climate	1	438	1	0.002 (0 -0.008)	-	-	-
	Oceanic climate	1	664	1	0.001 (0-0.005)	-	-	-
	Tropical rainforest climate	1	126	32	0.254 (0.182-0.333)	-	-	-
	Tropical savanna climate	1	30	4	0.133 (0.037-0.275)	-	-	-
	Total	5	1512	39	0.041 (0-0.217)	96	0.048	<0.001
Countries	Bangladesh	1	30	4	0.133 (0.037-0.275)	-	-	-
	Indonesia	1	126	32	0.254 (0.182-0.333)	-	-	-
	Iraq	1	254	1	0.003 (0-0.015)	-	-	-
	South Korea	1	438	1	0.002 (0-0.008)	-	-	-
	Switzerland	1	664	1	0.001(0-0.005)	-	-	-
	Total	5	1512	39	0.041 (0-0.217)	96	0.048	<0.001
Average temperature (°C)	10-20	3	1356	3	0.002 (0-0.005)	0	0	0.81
	>20	2	156	36	0.206(0-0.976)	57	0.006	<0.001
	Total	5	1512	39	0.041 (0-0.217)	96	0.048	<0.001
Humidity	40-75	5	1512	39	0.041 (0-0.217)	96	0.048	<0.001
	Total	5	1512	39	0.041 (0-0.217)	96	0.048	<0.001
Annual rainfall	< 400	1	254	1	0.003 (0-0.015)	-	-	-
	1001-1500	1	664	4	0.001 (0-0.005)	-	-	-
	> 1500	3	587	34	0.094 (0-0.645)	97	0.058	<0.001
	Total	5	1512	39	0.041 (0-0.217)	96	0.048	<0.001
Diphyllobothrium Spp/Diphyllobothrium latum	*Diphyllobothrium spp.*	1	438	1	0.002 (0-0.008)	-	-	-
	Diphyllobothrium latum	4	1074	38	0.059 (0-0.346)	97	0.055	<0.001
	Total	5	1512	39	0.041 (0-0.217)	96	0.048	<0.001

HDI: Human development index.

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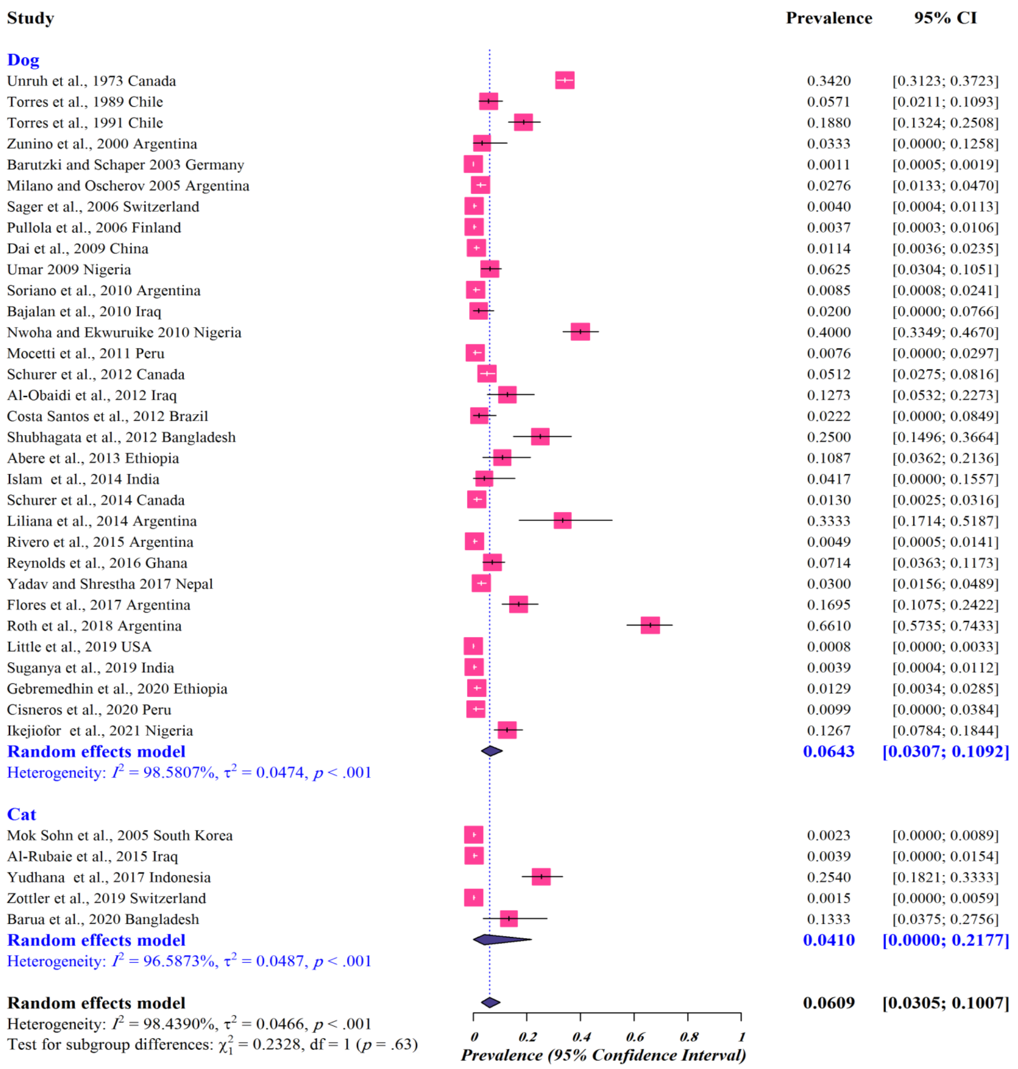

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Figure 2. Forest plots for random-effects meta-analysis of *Diphyllobothrium* in dogs and cats

(The boxes indicate the studies' effect size [prevalence] and the whiskers indicate its confidence interval for the corresponding effect size. No specific difference is observed between white and black bars, only studies with a very narrow confidence interval are shown in white. In the case of diamonds, their size indicates the effect size, and their length indicates the confidence intervals).

in regions with tropical rainforest climate (0.254%, 95% CI, 0.182%-0.333%), the average temperature of >20°C (0.206%, 95% CI, 0%-0.976%), annual rainfall of >1500 mm (0.094%, 95% CI, 0%-0.645%), and humidity of 40-75 (0.041%, 95% CI, 0%-0.217%).

The pooled prevalence rate concerning the HDI was the highest for low-level countries (0.133%, 95% CI, 0.037%-0.275%) (Table 3). According to the included studies on cats, all diagnoses were conducted based on parasitology methods with a pooled prevalence of 0.041% (95% CI, 0%-0.217%) (Table 3).

Publication bias

Asymmetry of the funnel plot indicates that publication bias was present in studies on dogs (Egger's test: t=3.04, P=0.0049, and Begg's test: P=0.0086) and no statistical publication bias existed for studies in cats (Figure 3). Furthermore, asymmetrical Doi plots suggest the presence of publication bias for the prevalence in dogs and cats. Accordingly, major asymmetry was observed for dogs (LFK index=4.66), and cats (LFK index=3.77) (Figures 3 and 4).

Quality assessment

The quality assessment results indicated that among 37 studies, 21 studies had a total score of 7-9 points (high

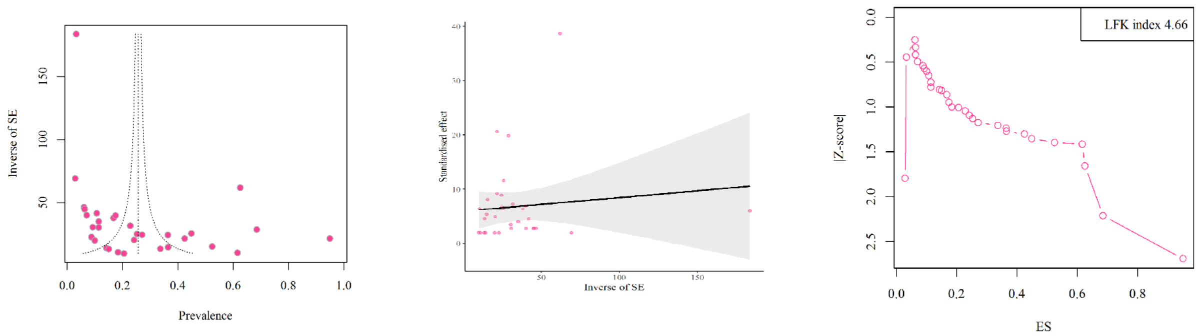

Figure 3. Egger funnel plot and begg's funnel plot to assess publication bias in studies evaluating *Diphyllobothrium* in dogs (A and B)

The middle line is the effect size and the other two lines are the corresponding confidence ranges. Doi plot (C) for the global prevalence of Diphyllobothrium in dogs. A Luis Furuya -Kanamori (LFK) index of 4.66 indicates major asymmetry.

quality), and 16 studies had a total score of 4-6 points (moderate quality) (Supplementary Table 1).

A QGIS map was created to represent the global prevalence of *Diphyllobothrium* parasites in dogs and cats based on included studies (Figure 5).

4. Discussion

To the best of our knowledge, this systematic review and meta-analysis is the first to evaluate the global prevalence of *Diphyllobothrium* infection in dogs and cats. We found that the overall estimate of the prevalence was 0.060%.

Due to the enormous number of stray dogs and cats with little or no documented history, it is essential to identify risk factors to establish an efficient control measure, particularly in developing countries [23-26]. Moreover, *Diphyllobothrium* infection in dogs and cats indicates contamination of human food sources (raw or undercooked fish) with these parasites [27, 28].

Furthermore, the consumption of traditional fish dishes, including sushi and sashimi, is very common in Southeast Asian countries and can be a potential source of diphyllobothriasis in humans [29, 30]. Our findings indicate that in Asia, *Diphyllobothrium* infection was most prevalent in cats, while in Africa, it was the highest in dogs. This inconsistency found for prevalence emphasizes that the risk of infection varies in each geographic region. *Diphyllobothrium* tapeworms have a broad host specificity, mostly observed in tropical and sub-tropical areas, with the highest prevalence in Southeast Asia and

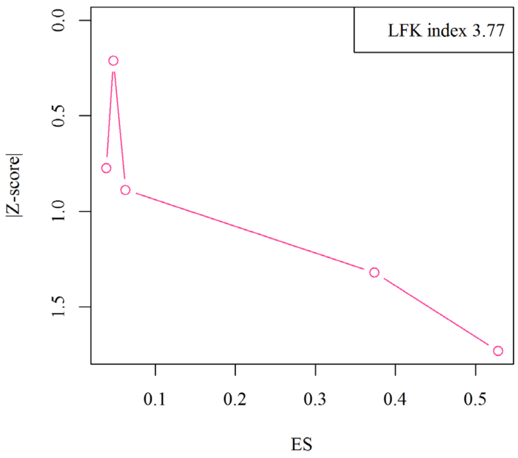

Figure 4. Doi Plot for the Global Prevalence of *Diphyllobothrium* in Cats A Luis Furuya -Kanamori (LFK) index of 3.77 indicates major asymmetry

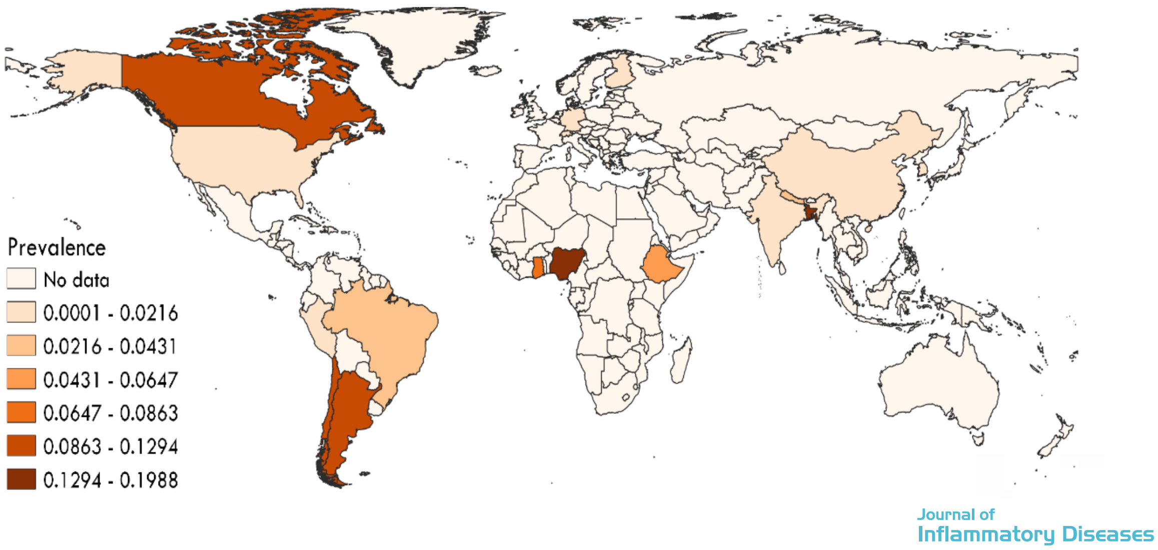

Figure 5. A QGIS map representing the global prevalence of *Diphyllobothrium* parasites in dogs and cats based on included studies

Africa [12, 31, 32]. This statement is consistent with the findings of the current study, suggesting that tropical climates are associated with the highest prevalence of *Diphyllobothrium* infection.

Asian countries account for 60% of the world's fish production, and approximately 13% of their food expenses are related to fish purchases [33]. We demonstrated that among different countries, Bangladesh and Indonesia were the most prevalent regions for infection in dogs and cats, respectively. Bangladesh ranks fifth in global aquaculture production after Indonesia and is one of the most appropriate areas for freshwater aquaculture due to its favorable agro-climatic conditions. Fish culture is the most common freshwater aquaculture practice in Bangladesh, with the total fish production estimated to be 3.41 million tonnes per year from 2012 to 2013 [34]. In Indonesia, the economy and industry are under the domination of fisheries, and more than 54% of the country's animal protein is supplied by fish or seafood [35].

One of the important factors supporting the maintenance of the natural cycle of zoonotic parasites, such as *Diphyllobothrium* is the contamination of the local aquatic environment with feces, which can be a result of the discharge of untreated sewage, as well as environmental contamination by stray and domestic animals, especially dogs and cats, as sources of infection [36]. Therefore, the role of dogs and cats in the spread of these parasites should not be neglected [37].

Our findings revealed that the highest pooled prevalence was related to countries with a low level of HDI. A large number of middle-to-low-income tropical countries are considered to have poor hygiene and considerable populations of stray dogs and cats [38-40]. The monitoring systems for food markets in low-income countries in Africa and Asia are not effective and have defects regarding the presence of risky foodborne parasites that can be transmitted through animal-derived foods, such as fish [41].

Concerning diagnostic methods, we found that the parasitology method was dominant in all of the studies (both on dogs and cats), except for one study on dogs with a molecular technique. Direct microscopic examination is the routine method for the identification of eggs and proglottid segments of *Diphyllobothrium* tapeworms in stool specimens. Radiological imaging using an intraduodenal injection of diatrizoic acid is a diagnostic approach to visualize *Diphyllobothrium* parasites attached to the duodenum. Besides, another nonspecific method exists to diagnose diphyllobothriasis, which includes the evaluation of the blood vitamin B12 level. As a consequence of morphologic similarities, specific diagnoses of different species of *Diphyllobothrium* tapeworms may be complicated, especially with conventional morphological methods [41, 42]. Thus, it is recommended that molecular methods frequently using mitochondrial cytochrome c oxidase subunit 1 gene (cox1), 18S rDNA, and Internal Transcribed Spacer (ITS) can be used as a complement to diagnostic techniques to detect these parasites at the species level [42, 43].

The present systematic review and meta-analysis should be understood in the context of its limitations, some studies were observed with low sample sizes, all included studies except for one case, use parasitology methods, which have lower sensitivity and specificity than molecular methods and cannot diagnose the parasites at the species level, although we included most studies in our analysis, still, a lack of data or noticeably fewer reports from some of the particular geographical regions can be observed, as well as, studies were likely published in languages other than English that were not included in this review. Despite these limitations, our study provides the most comprehensive estimates of the prevalence of *Diphyllobothrium* infection in dogs and cats from a global perspective.

5. Conclusion

Since *Diphyllobothrium* infection has a foodborne route, regular parasitological screening of fish served in restaurants and fisheries and supermarkets is required to identify possible sources of human infection. The best way to reduce the infection in definitive hosts, especially dogs and cats, is to dispose of fish waste properly. To prevent infection in humans, the consumption of raw or undercooked fish should be avoided. As well, practices regarding food safety, including sufficient cooking of fish and freezing fish at -18oC for 24 to 48 hours, should be considered. In addition, control strategies such as surveillance of water contamination throughout the world, deworming of infected dogs and cats, and raising awareness for travelers and locals in endemic areas are needed to limit the spread and acquisition of infection.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Authors' contributions

Conceptualization: Aida Vafae Eslahi and Milad Badri; Methodology, software, validation, formal analysis: Meysam Olfatifar; Investigation, resources, and data curation: Fatemeh Barikbin, and Leila Zaki; Writing--review & editing, visualization, supervision, project administration: Aida Vafae Eslahi and Milad Badri; Funding acquisition: Milad Badri.

Conflict of interest

The authors declared no conflict of interest.

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Supplementary Table 1. Quality assessment using the newcastle-ottawa scale modified for cross-sectional studies

Row	Authors	Selection (Maximum of 5 Stars)	Comparability (Maximum of 2 Stars)	Outcome (Maximum of 3 Stars)	Total Scores
1	Unruh et al. 1973 [44]	**	**	*	5
2	Torres et al. 1989 [45]	**	*	**	5
3	Arenas et al. 1991 [46]	**	*	**	6
4	Zunino et al. 2000 [47]	**	**	***	7
5	Barutzki and Schaper 2003 [48]	***	*	***	6
6	Milano and Oscherov 2005 [49]	***	*	***	7
7	Sager et al. 2006 [50]	***	**	***	8
8	Pullola et al. 2006 [51]	***	*	***	6
9	Dai et al. 2009 [52]	***	**	**	5
10	Umar 2009 [53]	***	*	***	7
11	Soriano et al. 2010 [54]	****	*	***	8
12	Bajalan et al. 2010 [55]	***	*	***	7
13	Nwoha and Ekwuruike 2010 [56]	***	*	**	6
14	Mocetti et al. 2011 [57]	***	*	***	7
15	Schurer et al. 2012 [58]	****	*	***	8
16	Al-Obaidi et al. 2012 [59]	***	*	***	7
17	Santos et al. 2012 [60]	***	**	***	8
18	Das et al. 2012 [61]	***	**	***	6
19	Abere et al. 2013 [62]	****	**	**	8
20	Islam et al. 2014 [63]	**	**	**	6
21	Schurer et al. 2014 [64]	**	**	**	5
22	Semenas et al. 2014 [37]	***	*	**	6
23	Rivero et al. 2015 [1]	***	*	**	6
24	Amissah-Reynolds et al. 2016 [23]	***	*	***	7
25	Yadav and Shrestha 2017 [65]	****	*	***	8
26	Flores et al. 2017 [66]	***	*	***	7
27	Roth et al. 2018 [5]	**	*	**	8
28	Little et al. 2019 [67]	**	**	**	5
29	Suganya et al. 2019 [68]	**	**	**	6
30	Gebremedhin et al. 2020 [69]	****	*	***	8
31	Cisneros et al. 2020 [70]	****	**	***	9
32	Ikejiofor et al. 2021 [71]	****	*	**	8
33	Sohn et al. 2005 [72]	**	**	***	7
34	Al-Rubaie et al. 2015 [73]	**	**	**	6
35	Yudhana et al. 2017 [74]	**	**	**	5
36	Zottler et al. 2019 [75]	****	**	***	9
37	Barua et al. 2020 [76]	****	**	**	8

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*Indicates one criteria was followed; ** two criteria were followed; ***three criteria were followed; ****four criteria were followed;***** five criteria were followed.