Prevalence of zoonotic and non-zoonotic genotypes of *Giardia intestinalis* in cats: a systematic review and meta-analysis

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SUMMARY

There are no meta-analyses specifically describing the prevalence of zoonotic and non-zoonotic genotypes of *Giardia intestinalis* in cats, which would be useful in defining the importance of cats as a source of zoonotic transmission. We performed a systematic review of the literature in three databases (PubMed, Scopus and SciELO) to assess the proportion of cats that were infected with specific *G. intestinalis* genotypes. A meta-analysis using a random effects model was performed to calculate the pooled prevalence and 95% confidence intervals (95%CI). A 2-tailed alpha level of 5% was used for hypothesis testing. Measures of heterogeneity, including Cochran's Q statistic, the I^2 index, and the tau-squared test, were estimated and reported. Subgroup analyses were conducted by geographic area and animal origin, as well as coinfection. Publication bias was assessed using a funnel-plot.

Up to November 1, 2015, the literature search yielded 780 articles, of which 29 studies were valid for analysis. The pooled prevalence rate was higher for genotype F (19 studies, n=368 cats) with 55.8% [95%CI (42.8%-68.7%), τ^2=0.0463]. For genotype A (21 n=409) it was 38.7% [95%CI (29.0%-48.4%), τ^2=0.0527], for genotype D (7, n=276) 8.9% [95%CI (2.1%-15.8%), τ^2=0.0024], for genotype C (2, n=212) 3.1% [95%CI (2.5%-3.5%), τ^2=0.0001], for genotype E (3, n=187) 2.9% [95%CI (0.0%-8.1%), τ^2=0.0009], and for genotype B (4, n=230) it was 2.8% [95%CI (0.0%-5.7%), τ^2=0.0002]. Genotypes A and B of *G. intestinalis* are present in a wide range of hosts, including humans and cats, whilst genotype E has been reported in bovines, ovines, caprine and porcine animals, as well as in dogs and cats; and genotype F is almost exclusive to cats.

Thus genotypes A and B are the most important for zoonotic transmission. In this study, after genotype F (55.8%), genotype A yielded more than 38% in cats (95%CI 29-48). This has interesting possible implications in zoonotic transmission of giardiasis between cats and humans.

Keywords: parasite, zoonosis, epidemiology, genetic variation.

INTRODUCTION

The risk of transmission of zoonoses such as giardiasis is high, since the contact between humans and cats is progressively more intimate [1]. Because of this, it has become more relevant

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from the perspective of public health and epidemiological control, as evidenced in 2004, when giardiasis was included in the "Neglected Diseases Initiative of the WHO" to have a strategy to prevent and control the transmission of this infection across human and animal species [1, 2]. Besides being one of the most associated parasites regarding diseases of the gastrointestinal tract, with symptoms such as vomit, acute chronic diarrhea, malabsorption syndrome and weight loss in humans and animals, it has not been studied in all the required details, but it is certainly considered potentially zoonotic [3-7].
In this setting, there are no meta-analyses specifically describing the prevalence of zoonotic and non-zoonotic genotypes of *Giardia intestinalis* in cats, which would be useful in defining the importance of cats as source of such zoonotic transmission.

MATERIALS AND METHODS

Literature search
A systematic literature search in MEDLINE (PubMed / Index Medicus), Scopus (Elsevier) and SciELO (Scientific Electronic Library Online, NLM) data was performed in order to identify potentially relevant articles using the search strategy (giard* cat and giard* cats). The search was limited to articles in English, Spanish and Portuguese, without setting a limit for the year of publication of studies.

Eligibility and selection of studies
The original studies in which genetic characterization of *Giardia intestinalis* in infected cats was performed were included.

The papers that were repeated in the three databases were excluded at first. Later on, articles obtained were analyzed by their titles and abstracts in order to identify possible eligible studies for all the authors. The full text of possible papers for selection was reviewed in detail. Case control studies, case reports and those in which no prevalence of infection or genotype were evaluated were excluded. Finally, those studies in which no genetic characterization of *Giardia intestinalis* was made were discarded (Figure 1) [1-30].

Data extraction and quality assessment
Papers selected for inclusion in the meta-analysis were subjected to a thorough review, to later ex-

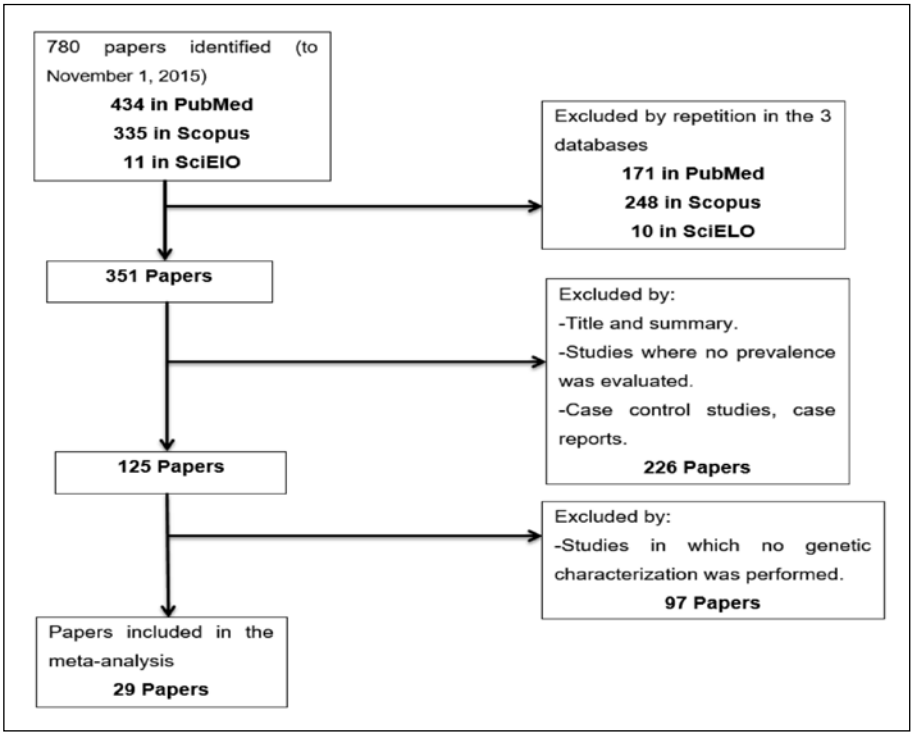

Figure 1 - Search strategy for identification of articles (Flow chart).

tract from them all the relevant data which was later verified by a third member. Data extracted included: title, country, year of sample collection, publication year, origin of animals, marker used for genetic characterization, number of infected cats, genotype presented in genotypic monoinfection, genotype presented in genotypic coinfection and sum of genotypes present in genotypic mono and coinfection. All extracted data were verified in a third round of review. The quality assessment of the studies was specifically carried out using the criteria of the STROBE Statement for quality assessment of studies included in metaanalysis [31]. For the management of bibliographic references the software EndNote 7.0® was used.

Data analysis

Metaanalyses were performed using Stata, version 11.0 and Microsoft Excel ® developed by Neyeloff et al., particularly for the forest plots. The combined prevalence and confidence intervals of 95% (95% CI) were used to summarize the effect of the size of each studyvariable group [32]. The random effects model was used, which was selected taking into account the initial characteristics of the studies, given the varying degree of heterogeneity in the data and given the inherent heterogeneity is in a systematic review of studies published in the literature of this type. An alpha level of 5% was used for the two-tailed hypothesis tests. They were estimated and reported heterogeneity measures, including Cochrane Q statistic, the index I^2 and tausquare (τ^2). Sub-analysis were made according to geographic areas, origin of animals and genotypic coinfection. Similarly, the frequency in which genetic markers were used in the different studies for genotyping *Giardia intestinalis* was measured. Publication bias was assessed using *funnelplot* (Figure 2). Ethical considerations are not directly applicable to this study. In addition, all procedures were applied according to good research practices and international standards for conducting metaanalysis, considering in principle the PRISMA standard for systematic reviews with or without metaanalysis.

RESULTS

Our literature search initially yielded 780 articles. The last day of search was November 1, 2015. After performing the exclusion for repetition in the 3 databases, 3351 articles were obtained. Later after titles and abstracts were analyzed and evaluated the full texts of possible eligible papers and excluding case control studies, case reports and those in which no prevalence of infection or genotype was evaluated, 125 items were obtained. In the end, from the 125 articles, 97 were excluded for not performing genetic characterization of *Giardia intestinalis*. Out from the total, 29 articles were considered eligible for inclusion in the metaanalysis. The details of the selection process of el-

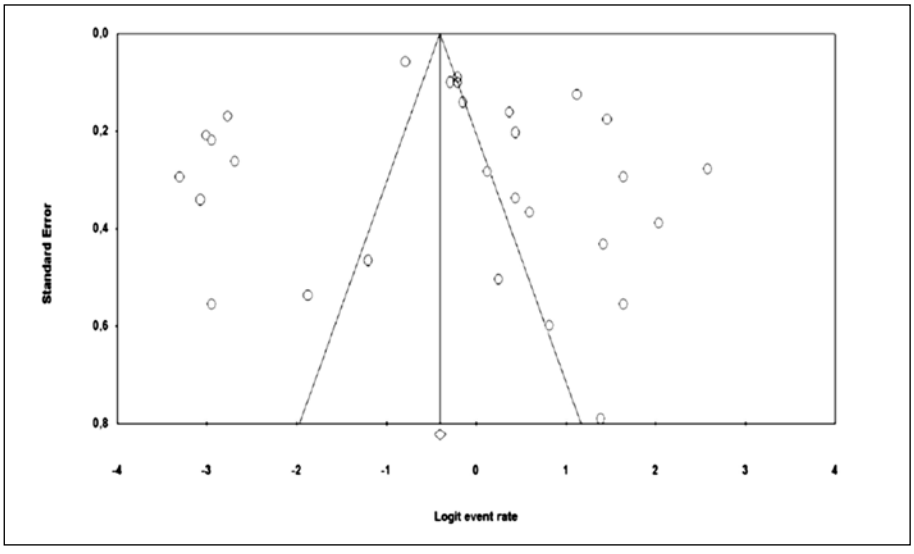

Figure 2 - *Funnel-plot* standard error event rate (Logit) to assess publication bias.

igible papers are summarized and presented in a flow chart (Figure 1).

The studies included in the analysis were published between 2004 and 2015 and reported data on 449 animals (159 were pets, 12 street animals, 13 came from shelters, 9 from breeding catteries, 1 from a pet shop and 255 from unknown origin) (Table 1). Seven of the studies were conducted in the Americas, 16 in Europe and 6 in AsiaPacific (Table 1).

Gdh genotypic markers were used in 58.62% of the selected studies (17/29), βgiardin in 44.82% (13/29), tpi in 24.13% (7/29), 18 SrDNA in 20.68% (6/29), SSUrDNA by 17.24% (5/29) and SSUrRNA in 17.24% (5/29). Genotypes A, B, C, D, E and F were found in genotypic monoinfection and the coinfection of AC, AD, AF, AFD, BD, BF, CD and ED genotypes were found (Table 2). Given the objective of this research, the sub groups of genotypes (AI, AII, AIII, BIV), distinguished in

Table 1 - General characteristics of the included studies.

Origin of the samples											
Year (Publication)	*Country*	*Year of collection*	*N*	*Pets*	*Stray Cats*	*Shelter Cats*	*Cattery Cats*	*Pet Shop Cats*	*Indeterminate Cats*	*Score*	*Reference*
2015	Austria	2013	17						17	18	[1]
2015	Australia	2010-2011	11						11	17	[2]
2015	China	2013	10			10				18	[3]
2015	China	2013	1					1		17	[4]
2015	Germany	2009-2012	53	53						19	[5]
2015	Norway	2012	9				9			18	[6]
2015	Canada	*	8						8	17	[7]
2014	Italy	*	11	11						17	[8]
2014	Italy	2010-2011	17	17						17	[9]
2013	Germany	2007	2	2						18	[10]
2012	United States	2005-2010	13						13	18	[11]
2012	Italy	2008-2010	1	1						19	[12]
2012	Spain	*	1			1				17	[13]
2011	Poland	2006-2007	6	6						16	[14]
2011	Canada	2008-2010	13	13						19	[15]
2011	Portugal	2007-2008	2			2				18	[16]
2011	Italy	2006-2009	6		6					18	[17]
2011	Italy	2006-2009	5	5						18	[17]
2010	Sweden	2002-2008	18	18						19	[18]
2010	Japan	2006-2010	1	1						17	[19]
2009	Netherlands-Italia	*	158						158	18	[20]
2009	Netherlands	2007	2	2						17	[21]
2008	Australia	*	8						8	19	[22]
2007	Italy	*	10	7	3					18	[23]
2007	United States	*	17	17						17	[24]
2007	Brazil	2004-2006	19						19	19	[25]
2006	Colombia	2005	3		3					17	[26]
2006	United States	*	6	6						19	[27]
2004	Australia	*	21						21	17	[28]

the studies were classified according to the highest genotype to which they belonged (Genotype A or B). Similarly, those studies in which monoinfection and coinfection of a genotype occurred simultaneously were analyzed by the sum of both.

The analyses were stratified according to the genotypes (monoinfection, coinfection, sum of genotypes), as well as origin of the animal (pet, street, shelter and indeterminate) and geographical areas (America, Europe, AsiaPacific) (Tables

Table 2 - Genotypic markers and genotypes found in the included studies.

Genotypic markers						*Genotypes monoinfection*						*Genotypes coinfection*								*Sum of Genotypes*						
gdh	β-*Giardin*	*tpi*	*ssu-rDNA*	*ssu-rRNA*	*18SrDNA*	*A*	*B*	*C*	*D*	*E*	*F*	*A-C*	*A-D*	*A-F*	*A-F-D*	*B-D*	*B-F*	*C-D*	*E-D*	*A*	*B*	*C*	*D*	*E*	*F*	*Reference*
	*	*				5					12															[1]
*	*				*	1					10															[2]
*	*	*			*	8					1															[3]
		*									1															[4]
*	*				*	14	2	1	3		16	1	1	9	2		4			27	6	2	6		31	[5]
*	*	*									9															[6]
	*					8																				[7]
*										2	9															[8]
				*		14			3																	[9]
*						2																				[10]
*	*	*				3			2		7							1				1	3			[11]
*						1																				[12]
*	*													1						1					1	[13]
*						2	2		2																	[14]
*	*			*		12	1																			[15]
				*		2																				[16]
			*			1					5															[17]
			*			2					3															[17]
*	*	*		*		5				1	12															[18]
*	*				*						1															[19]
*	*	*	*			68	3	5	3	2	77															[20]
					*	1					1															[21]
	*								1		7															[22]
				*		10																				[23]
*						6					11															[24]
*						8					11															[25]
			*								3															[26]
			*								6															[27]
*					*	9			7							2		2	1		2	2	12	1		[28]

3, 4 and 5). All studies that showed a minimum of adequate quality were considered for analysis on the basis of their rating on the STROBE Statement scale (Table 1).

According to the analysis, the combined prevalence of genotype F in monoinfection in 368 cats was 55.8% [95% CI (42.8%-68.7%), τ^2=0.0463] (Figure 3.1), of genotype A in 409 cats was 38.7% [95% CI (29.0%-48.4%), τ^2=0.0527] (Figure 3.2), of genotype D in 276 cats was 8.9% [95% CI, (2.1%-15.8%), τ^2=0.0024] (Figure 3.3), of genotype C in 211 cats was 3.1% [95% CI, (2.5%-3.5%), τ^2=0.0001] (Figure 3.4), of genotype E in 187 cats was 2.9% [95% CI (0.0%-8.1%), τ^2=0.0009] (Figure 3.5) and in genotype B in 230 cats was 2.8% [95% CI, (0, 0%-5.7%), τ^2=0.0002] (Figure 3.6) (Table 3).

Publication bias was assessed with *funnelplot* for the standard error of the event (logit), with no bias evidence (Figure 2). The *funnelplot* showed a symmetrical distribution of the studies at both ends and around the midline.

Meanwhile, in the subanalysis of coinfections it was possible to evaluate only the genotypes AC, AF, CD, since the others were found in only one study which precluded analysis. According to this, the combined prevalence of AF coinfection genotypes in 63 cats was 1.7% [95% CI (0.69%-2.71%)] of the CD genotypes in 54 cats were 0.87% [95% CI (0.07%-1.82%), τ^2=0.0001], and of the AC genotypes in 34 cats was 0.2% [95% CI (0.0%-0.58%), τ^2=0.0001] (Table 3).

After making the sum of the genotypes found in mono and coinfection, the combined prevalence of genotype D in 87 cats was 26.7% [95% CI (2.1%-51.3%), τ^2=0.0521], of genotype F in 54 cats was 5.85% [95% CI (4.52%-7.18%), τ^2=0.0001], of genotype A in 54 cats was 5.09% [95% CI (3.75%-6.44%)], of genotype B in 74 cats was 1.08% [95% CI (0.37%-1.78%), τ^2=0.0001], and of genotype

Table 3 - Outcomes in meta-analysis by genotypes (random effects models).

Genotypes	*Studies*	*N*	*%*	*Combined effect % (95%CI)*	*Q*[†]	*I², %*[‡]	τ^{2}[§]	*P*
Monoinfection								
Genotype F	19	368	81.9	55.8 (42.8-68.7)	14.98	83.3	0.0463	<0.001
Genotype A	21	409	91.1	38.7 (29.0-48.4)	22.40	85.6	0.0527	<0.001
Genotype D	7	276	61.4	8.9 (2.1-15.8)	6.84	33.5	0.0024	0.220
Genotype C	2	211	46.9	3.1 (2.8-3.5)	1.00	0.0	0.0000	0.584
Genotype E	3	187	41.6	2.1 (0.0-6.0)	2.02	25.7	0.0009	0.260
Genotype B	4	230	51.2	2.8 (0.0-5.7)	2.96	16.3	0.0002	0.310
Coinfection								
Genotypes A-C	2	63	14.03	0.2 (0.0-0.58)	1.00	0.0	0.0000	0.401
Genotypes A-F	2	54	12.02	1.7 (0.69-2.71)	1.00	-	-	-
Genotypes C-D	2	34	7.5	0.87 (0.07-1.82)	1.00	0.0	0.0000	0.8515
Sum of Genotypes								
Genotype A	2	54	12.02	5.09 (3.75-6.44)	1.00	-	-	-
Genotype B	2	74	16.48	1.08 (0.37-1.78)	1.00	0.0	0.0000	0.8165
Genotype C	3	87	19.37	0.49 (0.04-0.94)	5.69	0.0	0.0000	0.654
Genotype D	3	87	19.37	26.7 (2.1-51.3)	2.19	87.2	0.0521	0.038
Genotype F	2	54	12.02	5.85 (4.52-7.18)	1.00	0.0	0.0000	-

* 95%CI = Confidence interval of 95%;
[†] Q Cochrane statistic for heterogeneity
[‡] I2 index for the degree of heterogeneity.
[§] Tau square test for heterogeneity.
- Does not apply

C in 87 cats was 0.49% [95% CI (0.04%-0.94%), τ^2=0.0001] (Table 3).

The subanalysis by source of the animals allowed to analyze pets' prevalence of genotypes A, B, DE and F in monoinfection. Accordingly, the combined prevalence of genotype F in 113 cats was 55.7% [95% CI (35.6%-75.9%), τ^2=0.0469], of genotype A in 141 cats was 44.4% [95% CI (28.6% -60.1%), τ^2=0.0966], of genotype D in 76 cats was 9.4% [95% CI (0.0%-19.4%), τ^2=0.0052], of genotype E in 29 cats was 6.5% [95%, (0.0%-13.2%), τ^2=0.0001] and of genotype B in 72 cats was 5.8% [95 CI% (0.0%-13.4%), τ^2=0.0013] (Table 4). Furthermore, according to the studies considered it was only possible to analyze the genotypes A and F in monoinfection in stray cats, so that the combined genotype prevalence in 9 cats was 40% [95%, (0.0%-100%)] and of F genotype in 9 cats was 83.3% [95% CI (53.5%-100%)] (Table 4). Similarly, in refuge cats it was only possible to analyze the genotype A in monoinfection, where the prevalence of this genotype in 10 cats was 80% [95% CI (55.2%-100%)] (Table 4).

Finally, in animals whose origin was unknown, it was possible to analyze genotypes A, D and F in monoinfection and CD genotypes in coinfection. According to the above reported data, the combined genotype prevalence of F in 226 cats was

Table 4 - Outcomes in meta-analysis by animal origin (random effects models).*

Origin	*Studies*	*N*	*%*	*Combined effect % (95%CI)*	*Q*†	*I², %*‡	τ^{2}§	*P*
Pets Monoinfection								
Genotype F	8	113	79.75	55.7 (35.6-75.9)	4.52	76.7	0.0469	0.001
Genotype A	11	141	87.03	44.4 (28.6-60.1)	9.9	89.5	0.0966	<0.001
Genotype D	3	76	46.91	9.4 (0.0-19.4)	1.91	40.2	0.0052	0.188
Genotype E	2	29	17.90	6.5 (0.0-13.2)	1	0.0	0.0001	0.325
Genotype B	3	72	44.44	5.8 (0.0-13.4)	1.9	20.1	0.0013	0.135
Stray Cats Monoinfection								
Genotype A	2	9	75	40.0 (0.0-100)	1.00	-	-	-
Genotype F	2	9	75	83.3 (53.5-100)	1.00	-	-	-
Shelter Cats								
Monoinfection								
Genotype A	3	10	76.92	80.0 (55.2-100)	1.00	-	-	-
Indeterminate Monoinfection								
Genotype F	6	226	88.62	68.0 (50.8-85.1)	5.96	81.7	0.0353	<0.001
Genotype A	7	247	96.86	33.8 (19.6-48.1)	6.32	66.8	0.0149	0.01
Genotype D	4	200	78.43	12.6 (0.0-26.9)	2.42	74.3	0.0166	0.009
Coinfection								
Genotypes C-D	2	34	13.33	8.7 (0.0-18.2)	1	0.0	0.0001	0.851
Sum of Genotypes								
Genotype C	2	34	13.33	8.7 (0.0-18.2)	1	0.0	0.0001	0.851
Genotype D	2	34	13.33	38.7 (5.4-72.0)	1	0.0	0.0001	0.851

* 95%CI = Confidence interval of 95%;
† Q Cochrane statistic for heterogeneity
‡ I2 index for the degree of heterogeneity.
§ Tau square test for heterogeneity.
- Does not apply

68% [95% CI (50.8%-85.1%), τ^2=0.0353], of genotype A in 247 cats was 33.8% [95% CI (19.6%-48.1%), τ^2=0.0149] and of genotype D in 200 cats was 12.6% [95% CI (0.0%-26.9 %), τ^2=0.0166]. The combined prevalence of CD genotypes in 34 cats was 8.7% [95% CI (0.0%-18.2%), τ^2=0.0001]. The sums of genotype C and genotype D in 34 cats were 8.7% [95% CI (0.0%-18.2%), τ^2=0.0001] and 38.7 [95% CI (5.4%-72.0%), τ^2=0.0001], respectively (Table 4).

As the subanalysis made by geographical areas for the Americas it was possible to evaluate genotypes A and F in monoinfection. Accordingly, the prevalence of genotype F in 58 cats was 63.8% [95% CI (58.7%-69.0%), τ^2=0.0001] and genotype A in 70 cats was 47.2% [95% CI (23.7%-70.7%), τ^2=0.1162] (Table 5). On the other hand, in Europe, it was possible to analyze genotypes A, B, C, D, E and F in monoinfection and coinfection of the genotypes AF. According to the above reported data, the prevalence of genotype F in 279 cats was 53.3% [95% CI (39.1%-67.5%), τ^2=0.0268], genotype A in 297 cats was 37.5% [95% CI (27.1%-48.0%), τ^2=0.0259], genotype D in 234 cats was 4.6% [95% CI (0.0%-9.9%), τ^2=0.0017], genotype C in 211 cats was 3.1% [95%, (2.8%-3.5%), τ^2=0.0001], genotype E in 187 cats was 2.1% [95% CI (0.0%-6.0%), τ^2=0.0009] and genotype B in 217 cats

Table 5 - Outcomes in meta-analysis by geographic area (random effects models).*

Geographic Area	*Studies*	*N*	*%*	*Combined effect % (95%CI)*	*Q†*	*I2, %‡*	*τ 2§*	*P*
America Monoinfection								
Genotype F	5	58	73.4	63.8 (58.7- 69)	3.46	0.0	0.0001	0.823
Genotype A	5	70	88.6	47.2 (23.7- 70.7)	5.04	91.7	0.1162	<0.001
Europe Monoinfection								
Genotype F	9	279	87.7	53.3 (39.1-67.5)	7.20	75.0	0.0268	<0.001
Genotype A	13	297	93.39	37.5 (27.1-48.0)	12.43	74.5	0.0259	<0.001
Genotype D	7	234	73.5	4.6 (0.0-9.9)	3.56	54.2	0.0017	0.088
Genotype C	2	211	66.35	3.1 (2.8-3.5)	1.00	0.0	0.0001	0.584
Genotype E	3	187	58.8	2.1 (0.0-6.0)	2.02	25.7	0.0009	0.260
Genotype B	3	217	68.23	2.3 (0.0-4.8)	2.09	34.5	0.0004	0.217
Coinfection								
Genotypes A-F	2	54	16.9	17 (6.9-27.1)	1	-	-	-
Sum of Genotypes								
Genotype A	2	54	16.9	50.9 (37.5-64.4)	1	-	-	-
Genotype F	2	54	16.9	58.5 (45.2-71.8)	1	-	-	-
Asia-Pacific Monoinfection								
Genotype F	5	31	59.6	62.6 (7.9-100)	2.00	95.6	0.2135	<0.001
Genotype A	3	42	80.7	36.9 (1.1-72.8)	2.22	91.0	0.1128	<0.001
Genotype D	2	29	55.7	22.9 (2.4-43.3)	1	44.1	0.0096	0.181

* 95%CI = Confidence interval of 95%;
† Q Cochrane statistic for heterogeneity
‡ I2 index for the degree of heterogeneity.
§ Tau square test for heterogeneity.
- Does not apply

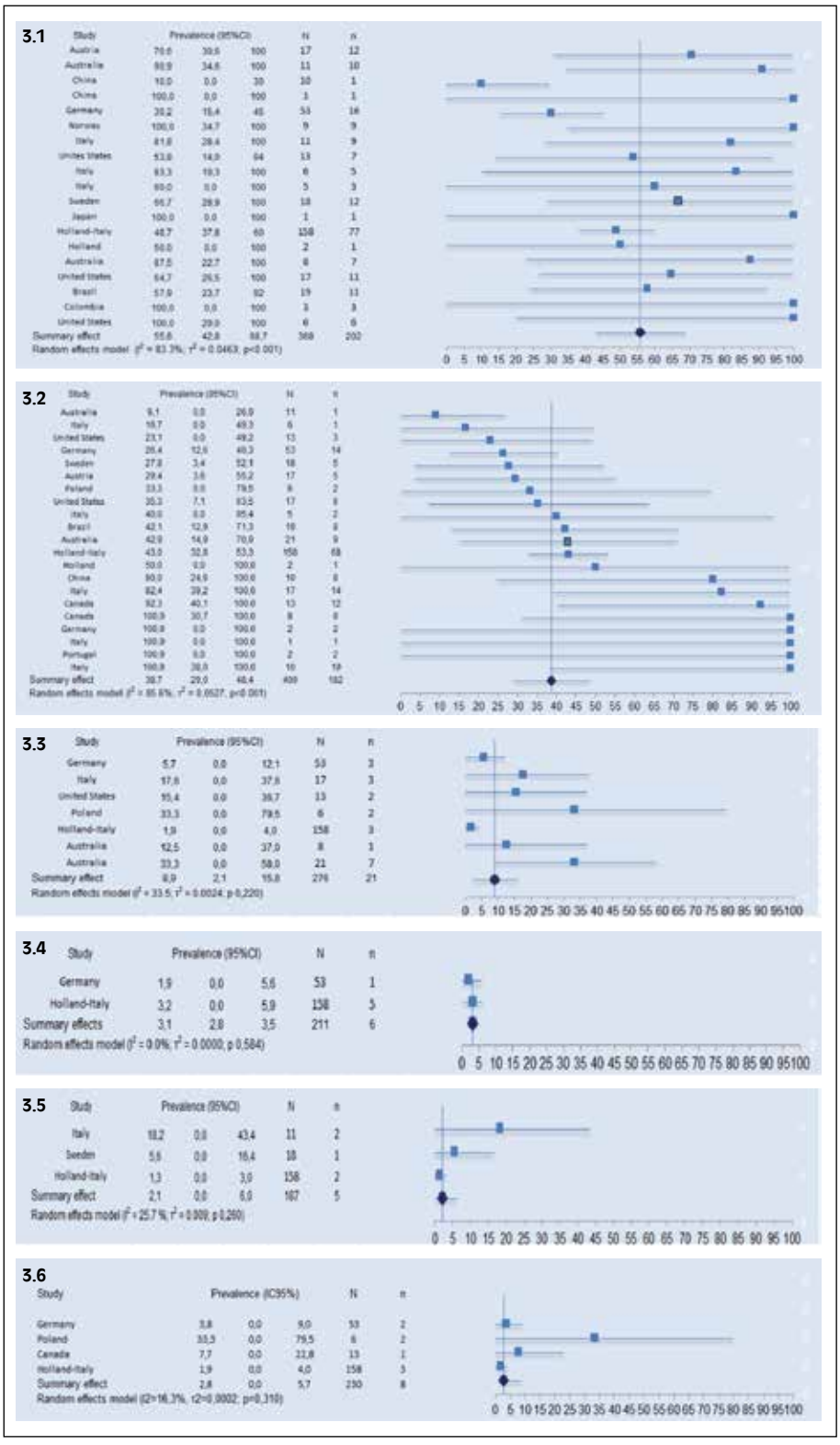

Figure 3 - Prevalence of genotypes, estimates (pictures) with confidence intervals of 95% (bars) for each select study; combined prevalence estimates are represented by diamonds in these graphs. **3.1.** Mono-infection genotype F. **3.2.** Monoinfection genotype A. Monoinfection genotype A. **3.3.** Monoinfection genotype D. **3.4.** Monoinfection genotype C. **3.5.** Monoinfection genotype E. **3.6.** Monoinfection genotype B.

was 2.3% [95% CI, (0 for 0%-4.8%), τ^2=0.0004]. The combined prevalence of genotypes AF in 54 cats was 17% [95% CI (6.9%-27.1%)]. The sum of genotype A in 54 cats was 50.9% [95% CI (37.5%--64.4%)] and of genotype F in 54 cats was 58.5% [95% CI (45.2%71.8%)] (Table 5). As for the Asia-Pacific region, it was possible to analyze genotypes A, D and F in monoinfection. On this basis, the genotype prevalence of F in 31 cats was 62.6% [95%, (7.9%-100%), τ^2=0.2135], genotype A in 42 cats was 36.9% [95% CI (1.1%-72.8%), τ^2=0.1128] and genotype D in 29 cats was 22.9% [95% CI (2.4%-43.3 %), τ^2=0.0096] (Table 5).

DISCUSSION

Giardiasis continues being a public health problem worldwide, since Giardia is the protozoan most related to diseases of the gastrointestinal tract in humans and one of the most common in domestic animals and wildlife [7, 10]. The findings of genotypes A and B in infected cats cause even greater concern because of the risk of zoonotic transmission that this represents. Studies in countries like Germany, Poland and Canada reported the presence in the three cases of genotypes A and B, emphasizing that all the animals were pets [2, 29]. On the other hand, in Brazil, two studies that evaluated samples from two communities that coexisted with pets, found the presence of genotype A in cats and people, indicating the possibility of cross-transmission [33, 34].

A recent metaanalysis conducted in the UK in which infection prevalence of giardiasis in cats of various geographic areas were analyzed, described a combined prevalence of 12% of cats infected by *Giardia intestinalis* [30]. However, in this study no prevalence of genotypes of the parasite were evaluated, so it was not possible to define the potential of zoonotic transmission from these animals. Unlike the present metaanalysis, there are not any other studies that have described the prevalence of zoonotic and nonzoonotic genotypes in cats or other animal species.

According to the results of this research, F and A genotypes in monoinfection were the most prevalent presented with 55.8% and 38.7% respectively. Other genotypes in monoinfection had no significant differences between them, which may be due in part to the limited number of studies that evaluated this and thus limited the statistical power of the analysis for these genotypes.

Although the genotype F was the most prevalent, results of genotype A imply that at least one third of infected cats that underwent genetic characterization of *Giardia intestinalis* were carriers of it, indicating possible implications for zoonotic transmission of the parasite between cats and humans. Similarly, due to the presence of a multiple variety of genotypes in this host, you should consider crosstransmission not only to humans but also among animal species.

In recent years the number of cats as pets has increased and its relationship to humans has become ever closer. Added to this, 60% to 80% of infected people develop this condition, so it is difficult to determine whether an individual is affected if he has no symptoms or an appropriate clinical diagnosis [22]. According to the above, and the fact that children by their curious nature are more exposed to infection by direct contact with pets, they can be affected in their growth, cognitive and nutritional development without an appropriate management of the disease [7, 21, 22].

For this reason, it becomes a priority to rethink the directions on treatment, prevention and control of this disease in cats by veterinarians, with the aim of reducing the risk of zoonotic transmission of the parasite.

Today, in the practice of veterinary medicine there is a tool for prevention and treatment: the vaccine composed of inactivated trophozoites. This allows the organism to create an immune response in the body against infection by this parasite, in addition to helping to reduce the parasitic load on the host and therefore the excretion of cysts to the environment [35]. However, its effectiveness is still controversial, since experimental studies to date in dogs and cats show conflicting results [36-39]. Such vaccine is commercially used in countries of the Americas such as the United States, but its use is still restricted in Europe [40].

Therefore, it is important to make new studies on the effectiveness of this vaccine, or to develop research on new vaccination strategies, which seek to create immunity against infection, and eliminate or reduce the parasite load in the infected animal. All this aimed to reduce and control the spread of this disease among humans and animals.

In the different studies included, the genetic characterization of *Giardia intestinalis* was performed

using a variety of genotypic markers, where the gene for glutamate dehydrogenase (gdh) was the most used in a 58.62% (17/29) of the studies, followed by the gene βgiardin, which was used in 44.82% (13/29) of the studies. Regarding variants of genotypes A and B (AI, AII, AIII, BIII and BIV), there is a lack of studies that reach the level of subgenotyping, aiming to provide more information about the relationship between the variants and their host, zoonotic transmission and dynamic potential.

The subanalysis for genotypes in coinfection did not show statistically significant results, which may be due to the lack of studies evaluating coinfections. It is for this reason that in the future there should be carried out further research to address differences in prevalence, transmission, diagnosis and disease severity between mono and coinfections.

As the results by source of animals, genotypes that had higher prevalence in the case of pets were genotypes F with 55.7% and A with 44.4% genotype in monoinfection. While not zoonotic genotype was the most prevalent in this case, it is important to recognize the results of genotype on the risk of zoonotic transmission between owners and their pets, as discussed above. However, one of the limitations of this subanalysis was the small number of studies that identified the genotypes of *Giardia intestinalis* in stray and shelter cats, preventing the proper assessment of the relationship of the prevalence of genotypes and the origin of the animals. Similarly, many of the studies did not report the origin of infected cats, which were qualified for the sake of the study as "undetermined".

According to the above reported data, the need for further studies of prevalence of genotypes in stray and shelter cats is evident in order to understand the implications between the environment in which the animal lives and the prevalence of certain genotypes.

The data of this metaanalysis comes from studies in countries in Europe, the Americas and the AsiaPacific region showing differences (although not statistically significant) between them, especially in the prevalence of genotypes A and F in monoinfection, with 53.3% of genotype F and 37.5% of genotype A in Europe, 63.8% of genotype F and 47.2% of genotype A in the Americas and 62.6% of genotype F and 36.9% of genotype A in the AsiaPacific region. This finding could be the result of a different number of animals being evaluated in different geographical areas, since most studies were conducted in developed countries of the European continent.

However, this draws attention to the importance of researching the prevalence of *Giardia intestinalis* genotypes in underdeveloped countries where prevalence rates are higher, in order to obtain information to assist the management, control and prevention of this disease.

It is important to note that our estimates may have limitations regarding the great heterogeneity of the studies included and due to the fact that the studies published in languages other than English, Spanish and Portuguese were not considered. However, beyond this the *funnelplot* suggests that there is no publication bias for this report. Furthermore, the quality assessment showed overall good quality of the included studies.

In consideration of these results, it is important to note that there is scarcity of research aimed at identifying genotypes of *Giardia intestinalis* in infected cats, especially in Latin America, where in countries like Colombia only a single study regarding the topic has been carried out [28]. Accordingly, it is necessary to develop research covering the points discussed in this metaanalysis, and thus broaden the information about zoonotic and nonzoonotic genotypes presented in cats or other animals, with the aim of understanding better the transmission dynamics of this zoonosis. It is also important to make studies that focus on the development of techniques for practical and affordable diagnostic for human and veterinary physicians in the daily application of evidence based medicine, aiming for timely and appropriate management of the prevention, control and treatment of this infection.

Pets showed a significant prevalence of zoonotic genotype A, which is significant for the definition of cat as possible transmitter of this disease, with consequent implications for public health.

Finally, further research is needed to determine links between the source of infected cats and the prevalence of zoonotic or nonzoonotic genotypes. Similarly, it is important to develop studies to make genotypic characterization of this parasite in samples of animals in Latin America, especially cats but also in other groups of animals.

Conflict of interest
All authors, no competing interests.

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