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PREVALENCE OF FASCIOLIASIS IN RUMINANTS OF THE WORLD — META-ANALYSIS

O. V. Kruchynenko*, S. M. Mykhailiutenko, M. O. Petrenko

Faculty of Veterinary Medicine, Poltava State Agrarian University,
Skovorody st., 1/3, Poltava, 36003 Ukraine
**Corresponding author*
E-mail: oleg.kruchynenko@pdaa.edu.ua

O.V. Kruchynenko (https://orcid.org/0000-0003-3508-0437)
S. M. Mykhailiutenko (https://orcid.org/0000-0001-6634-1244)
M. O. Petrenko (https://orcid.org/0000-0002-5275-9401)

Prevalence of Fascioliasis in Ruminants of the World — meta-analysis. Kruchynenko, O. V., Mykhailiutenko, S. M., Petrenko, M. O. — Among the gastrointestinal parasitoses, fascioliasis is one of the most common diseases in ruminants. *Fasciola* spp. is recorded on five continents of the globe, in more than 50 countries. The parasitizing trematode causes economic losses associated with a decrease in milk yield, body weight, and culling of affected carcasses and organs. In this study, we aimed to quantify the prevalence of fascioliasis among ruminants (cattle, sheep and goats) of the world in terms of the odds ratio according to the Mantel–Haenszel test (M–H). Online databases in English, Russian and Ukrainian languages were searched for publications from January 2002 to September 2020. This meta-analysis included 42 studies with ruminant hosts. Data on the spread of fascioliasis were collected from different continents of the globe: North and South America, Europe, Asia and Africa. The results of the study found that the overall prevalence of fascioliasis in cattle was 6.41 %, while in small ruminants it was only 2.03 %. The disease in cattle was recorded 1.48 times more often than in sheep and goats. Egger's regression test revealed no significant publication bias (P = 0.265). The results of the meta-analysis confirm that the causative agent of fascioliasis circulates mainly in the emerging countries. The updated data on fascioliasis will expand the screening strategy to maintain the health of farm ruminants and reduce economic losses.
Key words: prevalence; *Fasciola hepatica; Fasciola gigantica;* cattle; sheep; goats; meta-analysis.

Introduction

Fascioliasis is a widespread, often chronic trematodosis of mainly ruminants (cattle, sheep, goats), recorded on all continents of the globe (Dalton, 1999; Mas-Coma et al., 2005; 2009; Rinaldi, 2015) and causing significant economic losses to livestock farms (Jaja et al., 2017; Arbabi et al., 2018; Ouchene-Khelifi et al., 2018; Nyirenda, 2019; Arias-Pacheco, 2020). For example, global production losses due to fascioliasis alone amount to US $ 3.2 billion per year (Mehmood et al., 2017). Fascioliasis is also a zoonotic "neglected tropical disease" (WHO, 2013), which poses a significant risk to public health (Mas-Coma et al., 2014 a) and is, in some cases, lethal (Mas-Coma et al., 2014 b). According to global estimations, nearly 17 million people are infected worldwide (Mas-Coma et al., 2009).

The causative agents of fascioliasis are two species of trematodes of the genus *Fasciola*, *Fasciola hepatica* L., 1758 and *F. gigantica* Cobbold, 1855 *F. hepatica* has a worldwide distribution, while *F. gigantica* is found mainly in the tropical Asia and Africa (Torgerson and Claxton, 1999). In addition, it has been shown that both species can occur in subtropical regions and hybridize (Agatsuma et al., 2000; Mas-Coma et al., 2009; Peng et al., 2009; Aghayan et al., 2019). Interestingly, molecular biological analysis of *Fasciola* spp. in some cases indicates the absence of hybrid forms (Walker, 2008; Mirahmadi, 2018), while in other cases, these forms are present (Le et al., 2008; Peng et al., 2009; Amer, 2016).

The life cycle of *F. hepatica* and *F. gigantica* is dixenous. The first intermediate host is a pulmonary mollusk of the family Lymnaeidae (Mas-Coma and Bargues, 1997; Mas-Coma et al., 2014). The cercariae emerging from infected mollusks encyst in the external environment, mainly on plants. Infection of the final hosts occurs when eating plants with invasive adolescaria (Dalton, 1999).

The fascioliasis can be diagnosed using the classical methods of helminthological dissection (Skrjabin, 1928) scatological methods (Esteban et al., 1998; Cringoli et al., 2010; 2017; Al-Mamunet al., 2011; Carneiro et al., 2018; Zárate-Rendón et al., 2019), and enzyme-linked immunosorbent test systems, ELISA (Hillyer, 1999; Akca et al., 2014; Munita et al., 2019). It has been shown that both scatological and ELISA have similar resolution (George et al., 2019), which makes the previously obtained results comparable and allows for effective control of the prevalence of fascioliasis. Information on the prevalence of fascioliasis among different host species is highly controversial. Thus, in a number of cases, the prevalence rate of cattle was higher than that of sheep and goats (Sharma et al., 1989; Adediran et al., 2014; Jean-Richard et al., 2014; Kusumarini et al., 2020); in some cases it was, in contrast, lower (Akca et al., 2014; Tikuye, 2017); in other studies the rates did not differ (Yuan et al., 2016; Jones et al., 2016; Mokhber Dezfouli et al., 2016; Ayele et al., 2018).

The aim of this study was to conduct a meta-analysis of the distribution of *Fasciola* spp. in cattle and small ruminants (sheep and goats) in terms of the odds ratio based on a random effects model according to the Mantel–Haenszel criterion (M–H), which will make it possible to establish which species of animals is infected more often.

Material and methods

Information sources and search

The meta-analysis used the "Preferred reporting items for systematic review and meta-analysis" (PRISMA) recommendations (Moher, 2009). It was performed using ReviewManager (RevMan 5.4), certified freeware of Cochrane Collaboration (revman.cochrane.org). An in–depth search of publications was carried out in PubMed, GoogleScholar, ScienceDirect, SpringerLink, DOAJ, eLIBRARY.RU databases. Two authors independently searched for literature in English, Russian and Ukrainian. The search was carried out using the following keywords: *Fasciola hepatica*, *Fasciola gigantica*, cattle, sheep, goat, fascioliasis, prevalence.

Eligibility criteria, study selection and data collection

The exclusion criteria were: 1 — the study reported data on the detection of *Fasciola* spp. only for one host species or species that we did not include in the analysis (for example, buffalo); 2 — the total number of studies performed was less than 70 in each group; 3 — the exact number of positive cases in the surveyed animals could not be determined; 4 — publications duplicated each other. Subsequently, disagreements between the authors were resolved through discussion and consensus with the third author. Data for analysis were sampled in the period from January 2002 to September 2020. Our meta-analysis included 42 articles (fig. 1). Data on the spread of fascioliasis were collected from different continents of the globe: North and South America, Europe, Asia and Africa. The diagnosis was confirmed with tests of blood serum (ELISA), feces and posthumous (liver examination).

Analytical approach

The data in the meta–analysis, namely the number of positive cases among the examined animals of cattle and small ruminants (sheep and goats), were analyzed on the basis of a random effects model according to the Mantel–Haenszel test (M–H). The null hypothesis H_0 was that the number of cases of fascioliasis in cattle and small ruminants does not differ statistically, while the alternative hypothesis H_1 was that the fascioliasis is more common in a certain animal species. I^2 values of 25 %, 50 % and 75 % were considered as low, moderate, and high heterogeneity, respectively (Cochrane handbook). Effect size (ES) was defined as the odds ratio (OR = ad / bc) with 95 % confidence interval. For final analysis, all extracted data were entered into ReviewManager (RevMan 5.4) provided by the Cochrane Collaboration (revman.cochrane.org). 95 % confidence intervals were calculated in Open Source Epidemiologic Statistics for Public Health, Version 3.01, updated 2013/04/06 (www.OpenEpi.com). To determine the optimal estimate for frequencies and fractions, including for a small number of observations, the Wilson method was used (Wilson, 1927). Confidence interval values are given in parentheses.

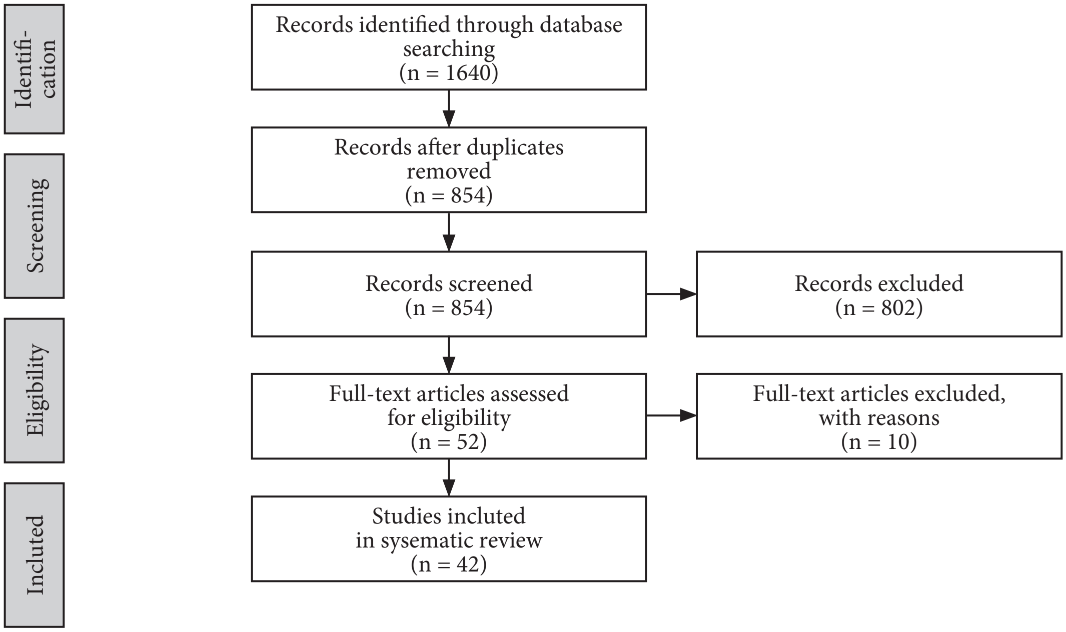

Fig 1. Flow diagram of the study design process.

Results

Table 1 presents the main characteristics of the included studies. According to the table 1, Iran, Ethiopia and Nigeria lead in the number of reported cases of fascioliasis in ruminants.

Table 1. Cases of prevalence of fascioliasis in ruminants in the world

Autor, year	Country	Method of diagnosis	Cattle Prev. (%), 95 % CI	Sheep Prev. (%), 95 % CI	Goats Prev. (%), 95 % CI
Abdolali et al., 2016	Iran	Microscopic	37.9 (31.32–45.1)	26.03 (20.9–31.9)	23.4 (17.7–30.8)
Abdulhakim et al., 2012	Ethiopia	Post mortem	28.6 (24.35– 33.4)	20.8 (17.1– 25.2)	13.5 (10.5–17.3)
Abraham, 2014	Nigeria	Microscopic	44.7 (39.9– 49.6)	–	36.0 (31.1– 41.2)
Adediran et al., 2014	Nigeria	Microscopic	54.3 (48.5– 59.9)	12.04 (9.3–15.4)	9.1 (6.7–12.14)
Aghayan et al., 2019	Armenia	Post mortem	15.7 (12.2– 20.1)	21.2 (19.41– 23.2)	44.4 (18.9– 3.3)
Akca et al., 2014	Turkey	ELISA	66.6 (62.35–70.6)	92.9 (90.5–94.83)	–
Al Mamun et al., 2011	Bangladesh	Microscopic	37.9 (36.4– 39.4)	30.9 (23.04–40.1)	32.0 (29.5–34.6)
Ali et al., 2011	Iran	Post mortem	2.4 (1.5–3.9)	6.9 (6.42–7.5)	4.1 (3.9–4.4)
Ayele et al., 2018	Ethiopia	Microscopic	62.3 (56.7– 67.63)	60.7 (54.9–66.2)	–
Choubisa & Jaroli, 2012	India	Microscopic	18.5 (12.7–26)	21.7 (14.2–31.7)	20.2 (13.34–29.4)
Cringoli et al., 2002	Italy	Microscopic	1.84 (1.2–2.9)	2.3 (1.45–3.6)	–

Dogo et al., 2017	Nigeria	Microscopic	6.83 (5.02–9.2)	11.6 (6.44–20.1)	2.83 (1.3–6.03)
Garg et al., 2009	India	Microscopic	10.8 (10.4–11.2)	2.8 (2.5–3.13)	2.35 (2.1–2.63)
Gazimagomedov et al., 2011	Russia	Microscopic	16.0 (11.6–21.71)	32.0 (25.93–38.7)	–
Huklaeva, 2009	Russia	Post mortem	19.2 (14.7–24.62)	25.6 (22.8–28.6)	17.5 (10.72–27.3)
Hussain et al., 2017	Iraq	Post mortem	1.6 (0.8–3.1)	2.9 (1.7–4.9)	–
Imani Baran et al., 2017	Iran	Microscopic	4.3 | (2.4–7.8)	3.5 (2.72–4.43)	–
Isah, 2019	Nigeria	Microscopic	45.7 (44.1–47.4)	38.7 (35.6–42.01)	35.0 (33.4–36.7)
Jean-Richard et al., 2014	Africa	Post mortem	68.5 (60.0–75.8)	22.7 (16.41–30.6)	12.01 (9.7–14.82)
Jones et al., 2016	UK	Microscopic	55.3 (44.1–65.92)	54.4 (44.2–64.34)	–
Kara et al., 2009	Turkey	Post mortem	5.4 (3.8–7.8)	4.42 (3.6–5.5)	–
Khoramian et al., 2014	Iran	Post mortem	3.7 (3.3–4.05)	3.3 (3.2–3.4)	2.8 (2.6–2.84)
Kitila et al., 2014	Ethiopia	Post mortem	25.9 (17.5–36.7)	7.1 (3.5–13.9)	0.92 (0.16–5.1)
Kordshooli et al., 2017	Iran	Post mortem	11.15 (10.6–11.7)	5.22 (5.02–5.44)	2.15 (2.1–2.23)
Koshevarov, 2011	Russia	Microscopic Post mortem	18.5 (15.2–22.4)	25.4 (20.6–30.9)	17.5 (11.8–25.02)
Kusumarini et al., 2020	Indonesia	Post mortem	29.8 (24.62–35.6)	8.03 (4.3–14.6)	5.7 (4.35–7.4)
Liba et al., 2017	Nigeria	Post mortem	12.0 (8.8–16.2)	9.0 (6.25–12.8)	7.3 (4.9–10.8)
Mohamadzadeh et al., 2016	Iran	Post mortem	1.81 (1.7–1.9)	2.3 (2.2–2.4)	0.05 (0.04–0.07)
Mokhber Dezfouli et al., 2016	Iran	Post mortem	1.9 (1.8–1.97)	1.92 (1.9–1.96)	–
Mungube et al., 2006	Kenya	Post mortem	25.7 (25.2–26.32)	5.2 (4.7–5.8)	6.6 (6.24–6.9)
Munguía–Xóchihua et al., 2007	Mexico	ELISA	24.4 (22.15–26.7)	30.4 (26.04–35.2)	42.9 (40.2–45.8)
Musotsi et al., 2017	Kenya	Post mortem	6.5 (6.3–6.8)	6.1 (5.9–6.3)	4.1 (3.82–4.4)
Ouchene-Khelif et al., 2018	Algeria	Post mortem	17.2 (16.21–18.2)	6.51 (5.9–7.15)	2.5 (2.15–2.9)
Piri et al., 2017	Iran	Post mortem	1.5 (0.9–2.5)	0.5 (0.4–0.6)	1.4 (0.9–2.1)
Sayadi et al., 2015	Iran	Post mortem	1.65 (1.6–1.74)	1.12 (1.1–1.15)	1.1 (1.06–1.14)
Shahbazi et al., 2016	Iran	Post mortem	1.5 (1.45–1.56)	0.8 (0.7–0.82)	0.7 (0.64–0.75)
Squire et al., 2018	Ghana	Microscopic	4.6 (2.6–7.4)	3.2 (1.3–6.5)	0.4 (0.1–1.9)
Taye et al., 2016	Ethiopia	Microscopic	36.7 (31.5–42.2)	48.3 (38.4–58.5)	–
Tikuye 2017	Ethiopia	Microscopic	9.52 (5.9–14.91)	37.6 (30.2–45.6)	6.8 (3.3–13.4)
Ullah et al., 2016	Pakistan	Microscopic	24.3 (15.75–35.5)	16.0 (8.3–28.5)	6.7 (1.8–21.3)
Zeleke et al., 2013	Ethiopia	Microscopic	69.9 (69.2–70.7)	35.0 (33.1–37.0)	27.1 (24.4–30.0)

A total of 579,258 specimens of cattle and 2,751,936 specimens of small ruminants (sheep and goats) were examined. Of these, 37,162 heads of cattle and 55,920 heads of sheep and goats were infected with fascioliasis (fig. 2).

Assessment of distribution and analysis of heterogeneity. High heterogeneity was found in the studies included in the meta-analysis, $I^2 = 99$ % ($P < 0.00001$). The results of the study established a general distribution of 6.41 % (6.35; 6.48) in cattle, while in small ruminants this indicator was, respectively, 2.03 % (2.01; 2.05). The fascioliasis in cattle was recorded 1.48 (1.19; 1.84) times more often than in sheep and goats. Since the 95 % confidence intervals do not include 1, the results can be considered statistically significant (overall effect: $Z = 3.55$; $P = 0.0004$).

In a meta-analysis of the spread of fascioliasis (fig. 3) in ruminants, publication error was not determined ($P = 0.265$).

	More prevalent in cattle		More prevalent in sh.& g			Odds Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Abdolali et al. 2016	71	187	103	413	2.5%	1.84 [1.27, 2.67]
Abdulhakim et al. 2012	110	384	132	768	2.6%	1.93 [1.45, 2.58]
Abraham 2014	179	400	126	350	2.5%	1.44 [1.07, 1.93]
Adediran et al. 2014	158	291	93	880	2.5%	10.05 [7.33, 13.78]
Aghayan et al., 2019	51	324	385	1803	2.5%	0.69 [0.50, 0.95]
Akca et al. 2014	333	500	502	540	2.5%	0.15 [0.10, 0.22]
Al Mamun et al. 2011	1571	4145	445	1394	2.6%	1.30 [1.14, 1.48]
Ali et al. 2011	16	666	1516	31288	2.3%	0.48 [0.29, 0.80]
Ayele et al., 2018	187	300	170	280	2.5%	1.07 [0.77, 1.50]
Choubisa & Jaroli, 2012	24	130	37	177	2.3%	0.86 [0.48, 1.52]
Cringoli et al., 2002	18	975	18	788	2.1%	0.80 [0.42, 1.56]
Dogo et al .2017	38	556	16	298	2.2%	1.29 [0.71, 2.36]
Garg et al. 2009	2465	22835	266	9563	2.6%	4.23 [3.72, 4.81]
Gazimagomedov et al. 2011	32	200	64	200	2.4%	0.40 [0.25, 0.65]
Huklaeva 2009	46	240	234	940	2.5%	0.72 [0.50, 1.02]
Hussain et al. 2017	8	500	13	448	1.8%	0.54 [0.22, 1.33]
Imani Baran et al., 2017	10	230	62	1782	2.1%	1.26 [0.64, 2.50]
Isah, 2019	1628	3560	1461	4080	2.7%	1.51 [1.38, 1.66]
Jean-Richard et al. 2014	89	130	104	748	2.4%	13.44 [8.80, 20.54]
Jones et al. 2016	42	76	49	90	2.2%	1.03 [0.56, 1.91]
Kara et al. 2009	28	513	78	1763	2.4%	1.25 [0.80, 1.94]
Khoramian et al. 2014	385	10462	7120	240863	2.7%	1.25 [1.13, 1.39]
Kitila et al. 2014	39	77	16	99	2.1%	5.32 [2.65, 10.69]
Kordshooli et al. 2017	1347	12079	5197	178198	2.7%	4.18 [3.92, 4.45]
Koshevarov 2011	83	448	91	398	2.5%	0.77 [0.55, 1.07]
Kusumarini et al., 2020	79	265	60	1008	2.5%	6.71 [4.63, 9.72]
Liba et al. 2017	36	300	49	600	2.4%	1.53 [0.97, 2.42]
Mohamadzadeh et al. 2016	545	29988	3112	237621	2.7%	1.39 [1.27, 1.53]
Mokhber Dezfouli et al. 2016	2615	137843	16724	867015	2.7%	0.98 [0.94, 1.02]
Mungube et al., 2006	6079	23606	1485	23779	2.7%	5.21 [4.90, 5.53]
Munguía-Xóchihua et al. 2007	328	1346	632	1580	2.6%	0.48 [0.41, 0.57]
Musotsi et al. 2017	2113	32385	3985	71836	2.7%	1.19 [1.13, 1.25]
Ouchene-Khelif et al., 2018	963	5608	547	11925	2.7%	4.31 [3.86, 4.82]
Piri et al., 2017	15	995	79	12612	2.3%	2.43 [1.39, 4.23]
Sayadi et al. 2015	1340	81012	6317	567982	2.7%	1.50 [1.41, 1.59]
Shahbazi et al. 2016	2834	188968	3715	474665	2.7%	1.93 [1.84, 2.03]
Squire et al., 2018	15	328	8	502	1.9%	2.96 [1.24, 7.06]
Taye et al. 2016	113	308	44	91	2.4%	0.62 [0.39, 0.99]
Tikuye 2017	16	168	63	252	2.2%	0.32 [0.18, 0.57]
Ullah et al. 2016	17	70	18	80	2.0%	1.10 [0.52, 2.36]
Zeleke et al. 2013	11096	15860	784	2237	2.7%	4.32 [3.93, 4.74]
Total (95% CI)		**579258**		**2751936**	**100.0%**	**1.48 [1.19, 1.84]**
Total events	37162		55920			

Heterogeneity: $Tau^2 = 0.46$; $Chi^2 = 4755.66$, $df = 40$ ($P < 0.00001$); $I^2 = 99\%$

Test for overall effect: $Z = 3.55$ ($P = 0.0004$)

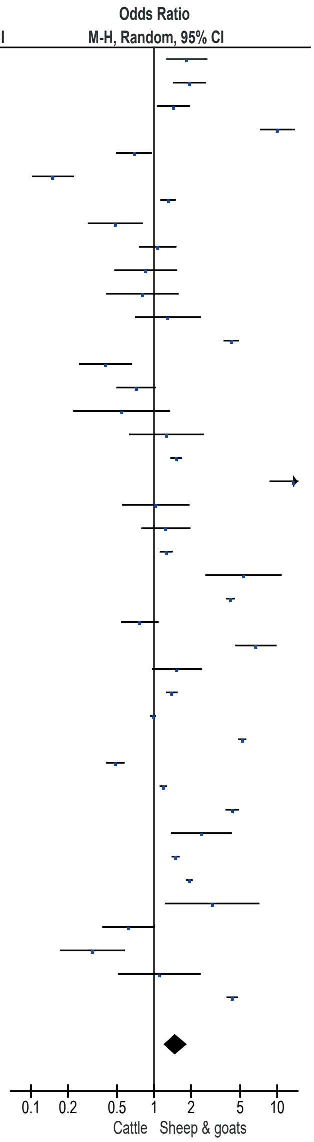

Fig. 2. Meta–analysis of the prevalence of fascioliasis in cattle and small ruminants (chosen measure of effect — odds ratio).

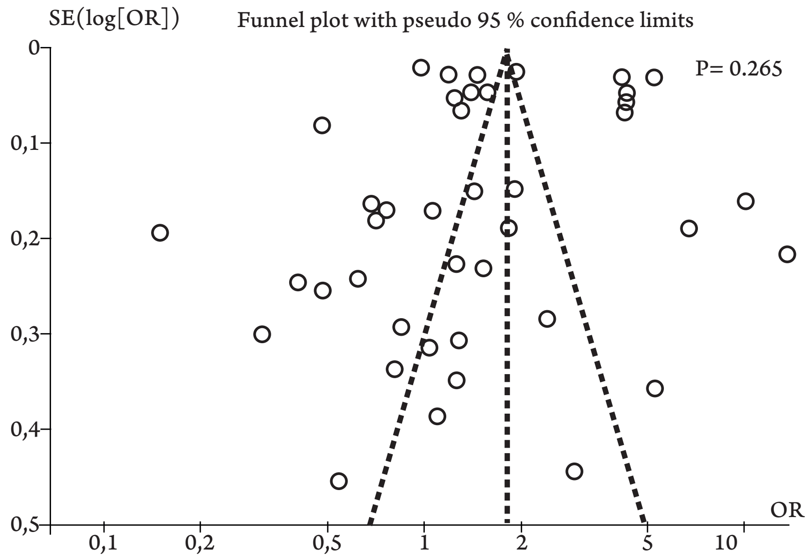

Fig. 3. Funnel plot for the binary result (chosen measure of effect — odds ratio). The x-axis denotes the prevalence of *Fasciola* spp. among ruminants, and the y-axis is the standard error of prevalence (P > 0.05 indicates no publication error).

Discussion

Most of the studies on meta-analysis and the spread of helminthiases among ruminants are concerned with research within the borders of one state or continent. Such studies can be focused on one disease, for example, fascioliasis (Khademvatan, 2019; Soosaraei, 2020) or a number of zoonotic helminthiases (Bennema et al., 2009; Fürst et al., 2012; Karshima et al., 2018).

We present the first meta–analysis of the spread of fascioliasis among ruminants in the world (cattle, sheep and goats). *Fasciola* spp. trematodes are found in more than 50 countries on five continents, especially in countries with developed animal husbandry. Karshima et al. (2018) conducted a meta–analysis, which found that the causative agent *Fasciola gigantica* had the widest geographical distribution in Nigeria. Systematic analysis for the period of 1999–2019 showed that the *Fasciola* infection in Iran was 6.2 % (Khademvatan et al., 2019). A lot of studies have shown that fascioliasis is more common in cattle (Garg, 2009; Abdulhakim et al., 2012; Adediran et al., 2014; Abdolali et al., 2016; Mehmood, 2017; Ghanimatdan et al., 2019; Kusumarini et al., 2020), and in some regions it is found only in cattle (Kruchynenko et al., 2020), but this has not been previously statistically proven. Our study clearly showed that the main final host for *Fasciola* spp. is cattle. Similar data, obtained by a group of researchers from Iran for the reporting period (2000–2016), confirm that the prevalence of fascioliasis in cattle is 21 %, and in sheep and goats it was at 2.4 % and 2 %, respectively (Soosaraei et al., 2020). At the same time, a number of studies have shown a higher prevalence of fascioliasis in sheep and goats (Munguía-Xóchihua et al., 2007; Huklaeva, 2009; Gazimagomedov et al., 2011; Taye et al., 2016). For example, the prevalence of that infection in Australia was 52.2 % in sheep and 26.5 % in cattle (Molloy, 2005). However, this is not a global trend and is most likely related to the type of animal housing (indoor or pasture), as well as the sample size in the studies.

Conclusions

Fascioliasis is an important trematodosis. We analyzed the published data for the period of 2002–2020 in order to update the global distribution and prevent economic losses. This disease is reported in ruminants all over the world. It is proved that the total geographic spread of fascioliasis among cattle was 6.41 % versus 2.03 % in small cattle (that is, higher in cattle by 1.48 times). Countries with higher prevalence, predominantly emerging countries, are a potential source of disease transmission and a threat to possible future outbreaks. The data presented are intended to improve the current understanding of the geographic distribution of the parasite and host range. The information provided will be useful for the application of more effective measures to combat fascioliasis in various geo-economic regions of the world.

Conflict of interest

The authors declare no potential conflicts of interests with respect to the research, authorship and/or publication of this article.

The current studies are the initiative of the authors and do not have any outside financial support. The research was carried out within the framework of the initiative topic for scientific work "Monitoring, improvement of diagnostics, treatment and prevention of invasive diseases of animals of the central part of Ukraine" (state registration No. 0112U001560).

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