American Journal of Animal and Veterinary Sciences

Review

Neospora caninum Infection in Cattle and Dogs in Iran: A Systematic Review and Meta-Analysis

[1]Mohammad Jokar, [2]Saied Bokaie, [3*]Vahid Rahmanian, [3]Razieh Zahedi, [3]Nader Sharifi and [4]Hekmatollah Khoubfekr

[1]Faculty of Veterinary Medicine, Karaj Branch, Islamic Azad University, Karaj, Iran
[2]Department of Food Hygiene and Quality Control, Division of Epidemiology and Zoonoses, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran
[3]Zoonoses Research Center, Jahrom University of Medical Sciences, Jahrom, Iran
[4]Iranshahr Health Services, Iranshahr University of Medical Sciences, Iranshahr, Iran

Article history
Received: 01-11-2020
Revised: 26-12-2020
Accepted: 23-01-2021

Corresponding Author:
Vahid Rahmanian
Zoonoses Research Center, Jahrom University of Medical Sciences, Jahrom, Iran
Email: vahid.rahmani1392@gmail.com

Abstract: Neosporosis, a parasitic infection caused by *Neospora caninum* (*N. caninum*), is one of the main contagious factors that cause reproductive disturbances in cattle and neuromuscular complaints in dogs. This review was performed to determine the prevalence of cattle and dogs neosporosis in Iran. Data were systematically gathered from January 2004 to July 2020 in the Islamic Republic of Iran from the following electronic databases: PubMed, Google Scholar, Science Direct, Scopus, Web of Science, Elmnet, Magiran, Irandoc, Iranmedex, Scientific Information Database (SID) and civilica. In cattle, 57 studies and in dogs 28 studies reporting the prevalence of neosporosis in different areas of Iran found which met our eligibility criteria. In total, the pooled prevalence of neosporosis, using a random-effect model, was estimated 24.2% (95% CI, 21.5-26.9) in cattle and 19.9% (95% CI, 15.3-24.4) in dogs. Furthermore, the majority of neosporosis cases were in the Southwest (37% in cattle and 30.6% in dogs) provinces of Iran. In conclusion, the pooled prevalence of cattle and dogs neosporosis in Iran is relatively high. This value differs among geographical regions as it is the maximum in the southwest for both and the minimum in the northeast for cattle and the southeast for dogs of Iran. These results are desirable for managing the control programs of this infection.

Keywords: Neospora, Bovine, Canine, Epidemiology, Prevalence, Iran

Introduction

Neospora caninum is an obligate intracellular apicomplexan protozoan parasite and recognized as the main cause of abortion in cattle and of neuromuscular complaints in dogs (Jin *et al*., 2017; Silva and Machado, 2016; Reichel *et al*., 2020). Domestic dogs, Australian dingoes, coyotes and gray wolf are can serve as both definitive and intermediate hosts of the *N. caninum* (Dwinata *et al*., 2018; Curtis *et al*., 2020), which shed many numbers of oocyst in their feces and contaminating the setting (Khan *et al*., 2020; Rocchigiani *et al*., 2017; Klein *et al*., 2019). Dogs and Intermediate hosts including cattle, horses, birds, goats, sheep, deers and buffaloes develop infected with the parasite by ingesting contaminated water or diet and by trans-placental infection. However, the protozoan can be transmitted to dogs of spring over several generations (Klein *et al*., 2019; González-Warleta *et al*., 2018; Fereig and Nishikawa, 2020). Vertical transmission is considered as the main road of spread and is critical for the maintenance of *N. caninum* in a bovine herd (González-Warleta *et al*., 2018; de Aquino Diniz *et al*., 2019).

In dogs, *N. caninum* caused different clinical signs according to age, breed and infected tissues; such as muscle atrophy, polymyositis, myocarditis, dermatitis, severe hepatitis, peritonitis, pneumonitis, stillbirths, neonatal deaths and neurological symptoms (Didiano *et al*., 2020; Decôme *et al*., 2019; Coelho *et al*., 2019; Moore and Venturini, 2018). However, *N. caninum* is deliberated as one of the important reasons for abortion in cattle; It follows sporadic, endemic and epidemic abortion patterns, being responsible for the economic burden in the cattle industry globally (Liu *et al*., 2020; de Oliveira *et al*., 2019). Other consequences are fetal death, resorption, mummification,

autolysis, stillbirth, or birth of clinically affected or normal calves but persistently infected (Dubey *et al*., 2017; Marugan-Hernandez, 2017).

The economic impacts of neosporosis in cattle herds are direct (abortion) and indirect (including earlier culling of seropositive cattle, costs of veterinary medical treatment and diagnosis of illness, decreased milk production, reduction in growth rates, etc.) (Liu *et al*., 2020; Demir *et al*., 2020). Although there are some reports on *N. caninum* infection's effects on milk production, many studies indicated that it may decrease in seropositive cows. Through, others reported milk production growths in seropositive cattle (Reichel *et al*., 2020; Chatziprodromidou and Apostolou, 2018).

In the context of this study focused on Iran, several studies reported that the prevalence of *N. caninum* in cattle and dogs. It is important to understand the epidemiology of cattle and dog neosporosis in all regions in Iran, to implement control and prevention programs that decrease the economic burden caused by the infection. This study is aimed to determine the overall prevalence of cattle and dog neosporosis in the Islamic Republic of Iran by systematic review and meta-analysis.

Materials and Methods

This study was designed as suggested via the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Liberati *et al*., 2009).

Bibliographic Search Strategy

All studies with epidemiological parameters are including the prevalence of *N. caninum* infection among cattle and dogs were the concern of this study. The relevant studies have been identified from January 2004 to July 2020 from five English sources i.e., Pub Med, Google Scholar, Science Direct, Scopus, Web of Science and five Persian databases namely, Elmnet, Civilica, Magiran, Irandoc and Scientific Information Database (SID). Dissertations (Theses) (n = 13) and Congress paper (n = 6) were collected from Irandoc and Civilica respectively. The selection process of studies is in view in the PRISMA Flowchart as shown in Fig. 1.

The search was implemented using the keywords as follows: Bovine, Canine, Cattle, Cow, Dog, Meat producing animal, *Neospora caninum*, Neospora, Neosporosis, Neosporosis in Animal, anti-Neospora antibodies, Epidemiology, Prevalence, Seroprevalence and Iran either alone or in combination and both Persian (Farsi) and English.

Data Collection

The titles and abstracts found in the search were independently reviewed by two of us as the authors, for checking inclusion and exclusion criteria. Differences of opinion between the specialists were resolved by a third person independently and consensus. All studies carried out to estimate the prevalence of neosporosis, detected by using different diagnostic approaches on cattle and dog were included. If studies were duplicates and not report *N. caninum* prevalence in cattle or dog were excluded.

The collected data for the present study were as follows: Time of publication, the first author, the geographical focus of the study, sample size, diagnostic tests, type of array in a diagnostic test and prevalence rate were extracted from the eligible studies. For this objective, an Excel data extraction form was used (Table 1).

Table 1: Papers met the eligibility criteria of this systematic review and meta-analysis

Authors	Year of publication	District	Province	Diagnostic test	Cut off point	Sample size	Total number of positive	Overall prevalence (%)
Hosseininejad *et al*.	2017	Center	Isfahan	ELISA	SIn > 0.153	1500	395	26.33
Nourollahi-Fard *et al*.	2017	Northeast	Razavi Khorasan	ELISA	PP ≥ 20	100	26	26.00
Morovati and Noaman	2016	Center	Isfahan	ELISA	S/P ≥ 0.5	611	196	32.10
Gharekhani *et al*.	2014a	West	Hamedan	ELISA	S/P ≥ 0.5	492	63	12.80
Heidari *et al*.	2014	West	Kurdistan	ELISA	S/P ≥ 0.5	368	29	7.80
Hadad Zadeh *et al*.	2010	North	Tehran	ELISA	S/P ≥ 0.5	768	298	38.80
Fard *et al*.	2008	Southeast	Kerman	ELISA	PP ≥ 20	285	36	12.60
Yousefi *et al*.	2009	North	Mazandaran	ELISA	S/P ≥ 0.5	237	76	32.00
Yagoob	2012a	Northwest	East Azerbaijan	ELISA	PP ≥ 20	236	42	17.70
Gharekhani and Heidari	2014	West	Hamedan	ELISA	S/P ≥ 0.40	1406	245	17.40
Sattari *et al*.	2011	Northeast	Golestan	ELISA	S/P ≥ 0.5	800	107	13.37
Nematollahi *et al*.	2011a	Northwest	East Azerbaijan	ELISA	SIn > 0.153	266	28	10.50
Hamidinejat *et al*.	2013	South	Fars	ELISA	S/P ≥ 0.5	178	95	53.30
Haji Hajikolaei *et al*.	2008	Southwest	Khuzestan	ELISA	S/P ≥ 0.5	557	117	21.00
Gharekhani and Tavoosidana	2013	West	Hamedan	ELISA	S/P ≥ 0.5	514	102	19.80
Razmi *et al*.	2006	Northeast	Razavi Khorasan	ELISA	AV > 0.2	337	156	46.29
Ansari-Lari *et al*.	2011	South	Fars	ELISA	AV > 0.2	169	98	58.00
Noori *et al*.	2019	Southeast	Sistan and Baluchestan	ELISA	S/P ≥ 0.5	184	7	3.80
Sadrebazzaz *et al*.	2004	Northeast	Razavi Khorasan	IFA	1.200	810	123	15.18
Ansari-Lari *et al*.	2017	South	Fars	ELISA	S/P ≥ 0.5	253	77	30.40
Gharekhani and Yakhchali	2019	West	Hamedan	ELISA	S/P ≥ 0.5	476	118	24.80
Nematollahi *et al*.	2011b	Northwest	East Azerbaijan	ELISA	S/P ≥ o.3	76	13	18.40
Adhami *et al*.	2014	West	Kurdistan	ELISA	S/P ≥ 0.5	336	64	17.60
Ranjbar *et al*.	2010	North	Semnan	ELISA	S/P ≥ 0.5	104	40	38.50

Table 1: Continued

Gharekhani *et al*.	2012	West	Hamedan	ELISA	S/P ≥ 0.5	400	80	20.00
Sabevarinejad *et al*.	2013	West	Lorestan	ELISA	S/P ≥ 0.5	181	50	27.62
Adhami *et al*.	2015	West	Kurdistan	IFA	1.200	410	69	16.82
Tavanaee and Namavari	2017	South	Fars	ELISA	S/P ≥ 0.5	184	59	32.07
Javanshir	2015	Center	Qom	ELISA	S/P ≥ 0.5	200	18	8.00
Atashgahi	2015	Northeast	Razavi Khorasan	ELISA	S/P ≥ 0.5	250	45	18.00
Asadi Karam	2016	Southeast	Kerman	ELISA	S/P ≥ 0.40	93	12	12.90
Forooghi	2013	West	Lorestan	ELISA	S/P ≥ 0.5	184	52	28.26
Ghahvei	2014	West	Kermanshah	ELISA	S/P ≥ 0.40	92	33	35.86
Motamedi Pour	2016	Southeast	Kerman	ELISA	S/P ≥ 0.5	150	14	9.30
Noaman and Nabinejad	2020	Center	Isfahan	ELISA	S/P ≥ 0.5	216	41	19.00
Jokar *et al*.	2018	Center	Qom	ELISA	S/P ≥ 0.5	83	20	25.00
Davasaz	2009	Northwest	East Azerbaijan	ELISA	S/P ≥ 0.5	370	68	18.50
Tavasolian *et al*.	2010	North	Semnan	ELISA	S/P ≥ 0.5	104	26	25.00
Kamkar-Salehi and Namavari	2017	South	Fars	ELISA	S/P ≥ 0.5	184	34	19.00
Shabani *et al*.	2017	Northwest	Qazvin	ELISA	S/P ≥ 0.5	160	40	21.00
Ansarifar	2011	North	Tehran	ELISA	S/P ≥ 0.5	210	35	17.00
Youssefi *et al*.	2010	North and Northwest	Ardebil, Semnan and Mazandaran	ELISA	S/P ≥ 0.5	46	3	7.00
Razmi *et al*.	2014	Northeast	Razavi Khorasan	ELISA	S/P ≥ 0.5	200	38	19.00
Nayebzadeh *et al*.	2015	West	Lorestan	ELISA	S/P ≥ 0.5	347	34	9.80
Namavari *et al*.	2012	South and Southwest	Fars, Khuzestan and Kohgiluyeh and Boyer-Ahmad	ELISA	S/P ≥ 0.5	56	22	39.28
Saber *et al*.	2010	Northwest	East Azerbaijan	ELISA	S/P ≥ 0.5	136	24	17.60
Ahmad *et al*.	2011	Northwest	East Azerbaijan	ELISA	S/P ≥ 0.5	32	7	20.00
Nemat and Jafari	2010	Northwest	East Azerbaijan	ELISA	S/P ≥ 0.5	IgG	116	23.00
Nematollahi *et al*.	2013	Northwest	East Azerbaijan	ELISA	S/P ≥ 0.5	IgG	76	14.00
Pazoki Plasht *et al*.	2008	North	Tehran	ELISA	S/P ≥ 0.5	150	26	17.33
Hamidinejat *et al*.	2015	Southwest	Khuzestan	ELISA	S/P ≥ 0.5	108	58	53.70
Binaee	2017	North	Semnan	ELISA	S/P ≥ 0.5	237	67	28.27
Moraveji	2012	South	Fars	ELISA	S/P ≥ 0.5	164	23	14.00
Shahidi	2018	Northeast	Razavi Khorasan	ELISA	S/P ≥ 0.5	280	45	16.08
Behnaz	2017	Southwest	Khuzestan	ELISA	S/P ≥ 0.5	280	87	32.07
Mohammad Ali Gol	2010	Southwest	Khuzestan	ELISA	S/P ≥ 0.5	178	95	53.30
Hatami	2014	Northeast	Razavi Khorasan	ELISA	S/P ≥ 0.5	638	190	29.90
Malmasi *et al*.	2007	North	Tehran	IFAT	1:50	100	33	33.00
Yakhchali *et al*.	2010	Northwest	West Azerbaijan	IFAT	1:50	135	36	26.60
Sharifdini *et al*.	2011	Northwest	Ardabil	ELISA	SIn ≥ 0.23	171	52	30.40
Gharekhani and Heidari	2014	West	Hamedan	ELISA	S/P ≥ 0.40	270	73	27.00
Yagoob	2012b	Northwest	East Azerbaijan	IFAT	1:50	100	31	31.00
Ghanavati	2015	Southwest	Khuzestan	IFAT	1:50	150	30	20.00
Pouramini *et al*.	2017	Center	Tehran	ELISA	S/P ≥ 0.5	42	1	2.22
Khanmohammadi and Fallah	2011	Northwest	East Azerbaijan	IFAT	1:50	384	41	10.60
Gharekhani *et al*.	2014b	West	Hamedan	IFAT	1:50	270	70	27.00
Haddadzadeh *et al*.	2007	North	Tehran	IFAT	1:50	103	20	19.40
Hosseininejad *et al*.	2010a	West and Central	Chahar mahal va Bakhtiari, Isfahan	IFAT	1:50	233	24	10.30
Hosseininejad and Hosseini	2011	West and Central	Chaharmahal va Bakhtiari, Isfahan Khuzestan	ELISA	S/P ≥ 0.5	548	159	37.90
Razmi	2009	Northeast	Razavi Khorasan	PCR	Gene- Nc5 genomic fragment	174	4	2.20
Hosseininejad and Hosseini	2019	Southwest	Khuzestan	ELISA	S/P ≥ 0.5	100	18	18.00
Raeisi	2009	West	Chaharmahal va Bakhtiari	IFAT	1:50	200	55	27.50
Hosseininejad *et al*.	2017	Center	Isfahan	ELISA	SIn > 0.153	113	20	17.69
Gharekhani *et al*.	2014a	West	Hamedan	ELISA	S/P ≥ 0.5	360	36	10.00
Gharekhani and Heidari	2014	West	Hamedan	IFAT	1:50	270	73	27.00
Gharekhani and Tavoosidana	2013	West	Hamedan	ELISA	S/P ≥ 0.5	454	93	20.50
Gharekhani and Yakhchali	2019	West	West Azerbaijan	ELISA	S/P ≥ 0.5	185	16	8.60
Javanshir	2015	Center	Qom	ELISA	S/P ≥ 0.5	50	2	4.00
Gharekhani *et al*.	2019	West	Hamedan	ELISA	S/P ≥ 0.5	180	9	5.00
Yakhchali *et al*.	2017	Northwest	West Azerbaijan	IFAT	1:50	137	17	12.40
Khordadmehr	2012	Southwest	Fars	ELISA	S/P ≥ 0.5	108	59	54.62
Hosseininejad *et al*.	2010b	West	Chaharmahal va Bakhtiari	IFAT	1:50	100	32	32.00
Yagoob	2012b	Northwest	East Azerbaijan	IFAT	1:50	100	31	31.00
Ghafarifar *et al*.	2014	West	lorestan	PCR	Gene- Nc5 genomic fragment	428	9	2.10
Keyhani	2017	Center	Isfahan	PCR	Gene- Nc5 genomic fragment	100	22	22.00

Year of the pub (year of publication), IFA (Indirect immunofluorescent Assay), ELISA (Enzyme-Linked Immunosorbent Assay), SIn (Sample Index values), PP (Percent Positivity), S/P (Sample to Positive ratios), AV (Absorbance Values), IgG (Immunoglobulin G)

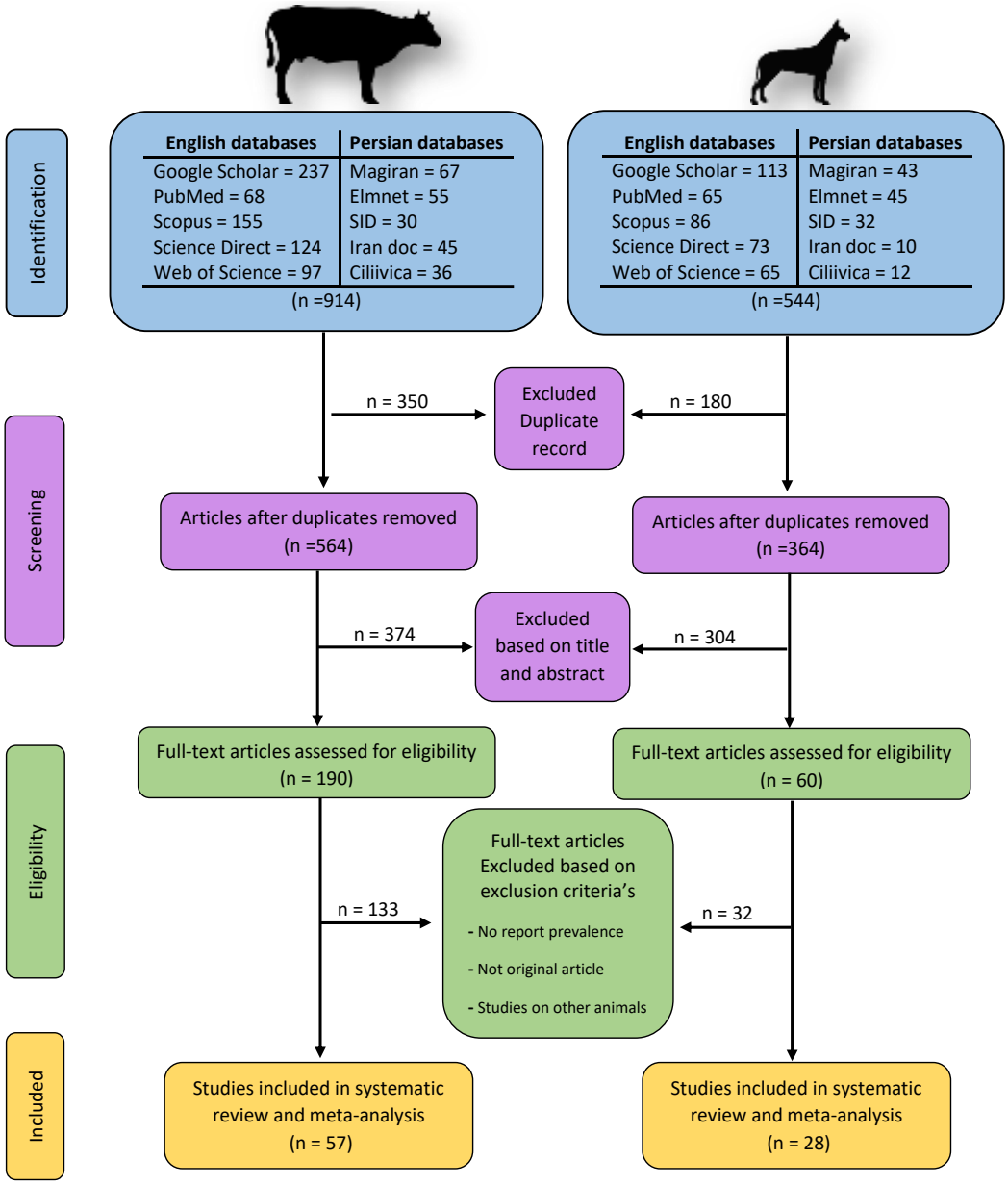

Fig. 1: Flowchart presenting the selection of articles analyzed in this systematic review and meta-analysis

Statistical Analysis

For this study, we supposed that the population under the study of included studies are random samples from a study population, therefore the random-effects model (DerSimonian and Laird, 2015; Cleophas *et al*., 2017), was also used to determine the overall prevalence of cattle and dog neosporosis. Proportions of individual studies, overall prevalence and the heterogeneity among studies were presented by forest plots. The heterogeneity was expected in advance and statistical methods, Cochran's Q test and I^2 index were used to assess the heterogeneity among the studies (Ruppar, 2020). The effects of probable factors in heterogeneity were evaluated by the meta-regression method. The Egger's regression and Begg's test and funnel plotting were used to assess publication bias.

The meta-analysis was performed with the trial version of StatDirect statistical software available from the public domain i.e., http://statdirects.com. To visualize the prevalence of cattle neosporosis in the different provinces of Iran. Furthermore, the Arc GIS 10.3 software was applied to map the distribution of neosporosis in different provinces of Iran.

DOI: 10.3844/ajavsp.2021.23.38

Results

In total, 1458 articles (914 for cattle and 544 for dogs) were found by searching the entire databases from 2004 to 2020; by systematic review and meta-analysis by considering the inclusion criteria. Of this, 85 studies (57 for cattle and 28 for dogs) has met the evaluation criteria of this study (Table 1).

A total number of 17,837 cattle and 5,565 dogs were examined for neosporosis in different geographical locations in Iran. In cattle and dogs, 4,118 and 1,066 cases, respectively, were detected positive using different detection tests as presented in Table 1. Data were extracted from twenty provinces in eight districts of Iran the distribution of reports in cattle and dogs is shown in Table 2.

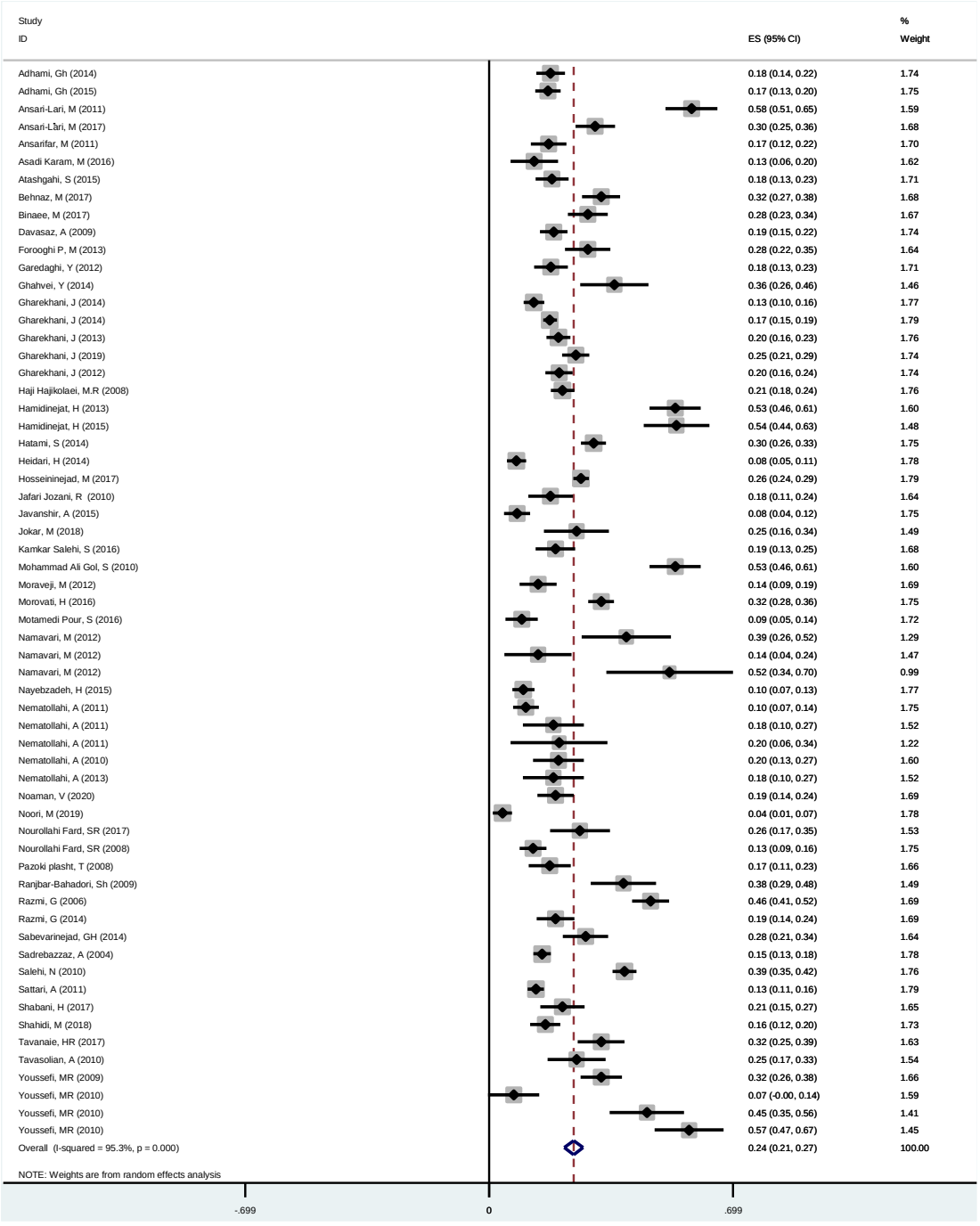

Fig. 2: Forest plot diagram showing portion meta-analysis plot of *N. caninum* infection prevalence in cattle in Iran (random-effects)

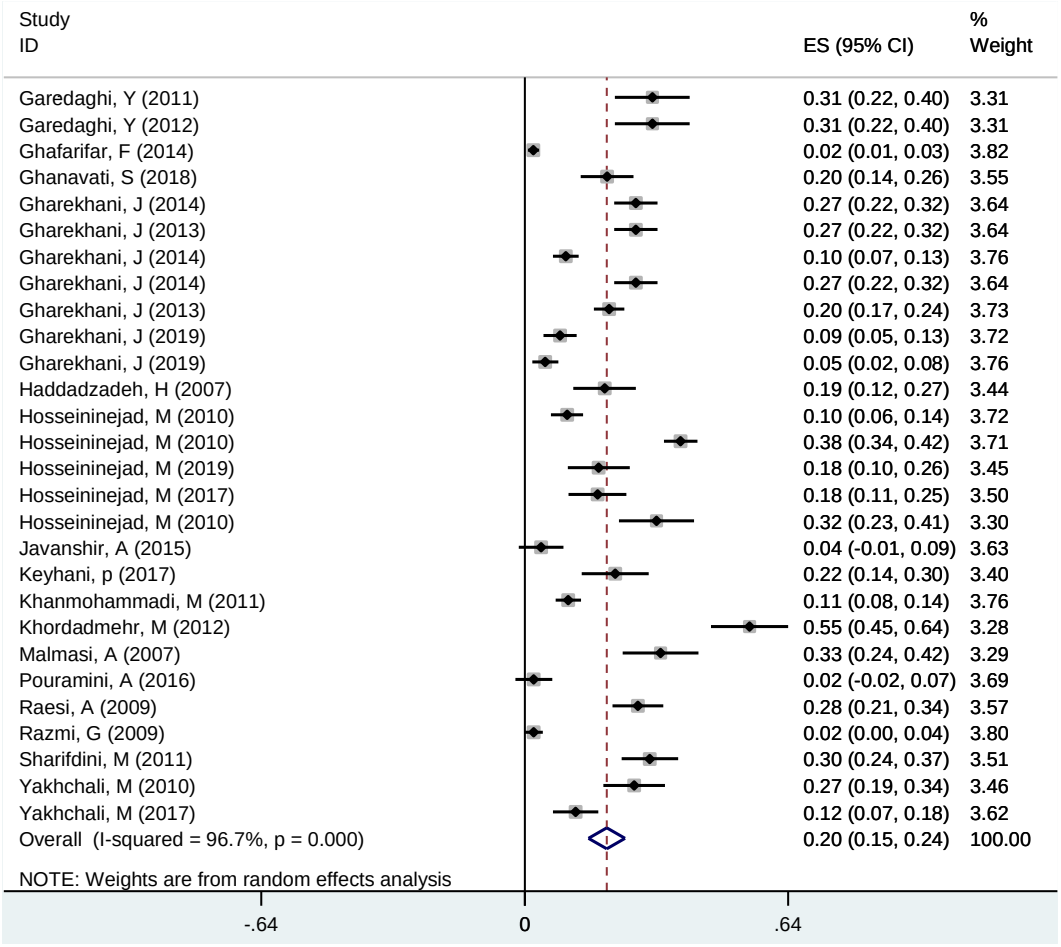

Fig. 3: Forest plot diagram showing portion meta-analysis plot of *N. caninum* infection prevalence in dogs in Iran (random-effects)

Table 2: Frequency of studies based on province

Province	Number of reports Cattle	Dog
Ardabil	1	1
Chaharmahal va Bakhtiari	1	3
East Azerbaijan	8	3
Fars	7	1
Golestan	1	-
Hamedan	5	6
Isfahan	3	4
Sistan and Baluchestan	1	-
Kerman	3	-
Kermanshah	1	-
Khuzestan	5	3
Kohgiluyeh and Boyer-Ahmad	1	-
Kurdistan	3	-
Lorestan	2	1
Mazandaran	2	-
Qazvin	1	-
Qom	2	1
Razavi Khorasan	7	1
Semnan	4	-
Tehran	3	3
West Azerbaijan	-	3

Three types of detection tests were employed to assess neosporosis infection in cattle and dogs as in the following: Enzyme-Linked Immunosorbent Assay (ELISA, 67 studies), Indirect Immunofluorescent assay (IFA, 15 studies) and polymerase chain reaction (PCR, 3 studies just in dog).

Overall, the pooled prevalence of neosporosis, using random-effects meta-analysis, among cattle and dogs was estimated at 24.2% (95% CI, 21.5-26.9) and 19.9% (95% CI, 15.3-24.4) respectively (Fig. 2 and 3). There was a high degree of heterogeneity in the prevalence estimates between different studies was observed in cattle, Q statistic = 1285.95 (df = 60), P<0.0001 and I^2 = 95.3% and in dog, Q statistic = 817.36 (df = 26), P<0.0001 and I2 = 96.8%.

Multivariate meta-regression analysis did not display any heterogeneity in dogs and publication year, province, detection method, testing cut-off levels and type of array in cattle studies (Table 3), but the district of studies in cattle might be the cause of heterogeneity (p = 0.029). Univariate meta-regression analyses indicated that Sample size of studies in cattle (p = 0·013) and

publication year of studies in dogs (p = 0·013) might be the cause of heterogeneity, while we identified no meaningful differences in detection method, testing cut-off levels, type of array, districts and province (Table 3).

Table 3: Result of Multivariate and Univariate meta-regression model for detecting probable sources of heterogeneity

	Cattle				Dog			
	Multivariate		Univariate		Multivariate		Univariate	
Probable source of heterogeneity	Coefficient	P-value	Coefficient	P-value	Coefficient	P-value	Coefficient	p-value
Year	-0.0092731	0.076	-0.0060815	0.225	-0.0105618	0.183	-0.0136308	0.041
Sample size	-0.0000236	0.722	0.0004783	0.041	-0.000152	0.426	-0.000023	0.904
Districts	-0.0166418	0.029	-0.0133732	0.065	-0.0318206	0.185	-0.0151036	0.329
Province	0.0023875	0.539	0.0041939	0.233	0.0184053	0.088	0.0020018	0.767
Detection method	-0.1722615	0.128	-0.0865771	0.358	0.0918528	0.480	-0.0640048	0.072
Testing cut-off levels	0.0177409)	0.395	0.0136295	0.434	-0.0248123	0.573	-0.0250503	0.075
Type of array	-	-	-0.0000541	0.364	-0.2381858	0.084	-0.1310803	0.085

Table 4: overall prevalence of neosporosis in different districts of Iran

	Cattle		Dog	
Districts	Pooled prevalence	5% Confidence interval]	Pooled prevalence	5% Confidence interval]
North	32.8	25.1-40.5	25.9	12.6-39.3
Northwest	16.5	13.5-19.5	23.2	14.6-31.8
Northeast	22.8	16-29.6	2.2	0-4.4
West	19.0	15.5-22.6	19.4	12.2-26.5
Center	22.0	13.3-30.7	11.0	1.9-20.1
South	35.0	22.5-47.4	-	-
Southwest	37.0	23.9-50.1	30.6	10-51.2
Southeast	9.3	4.3-14.3	-	-

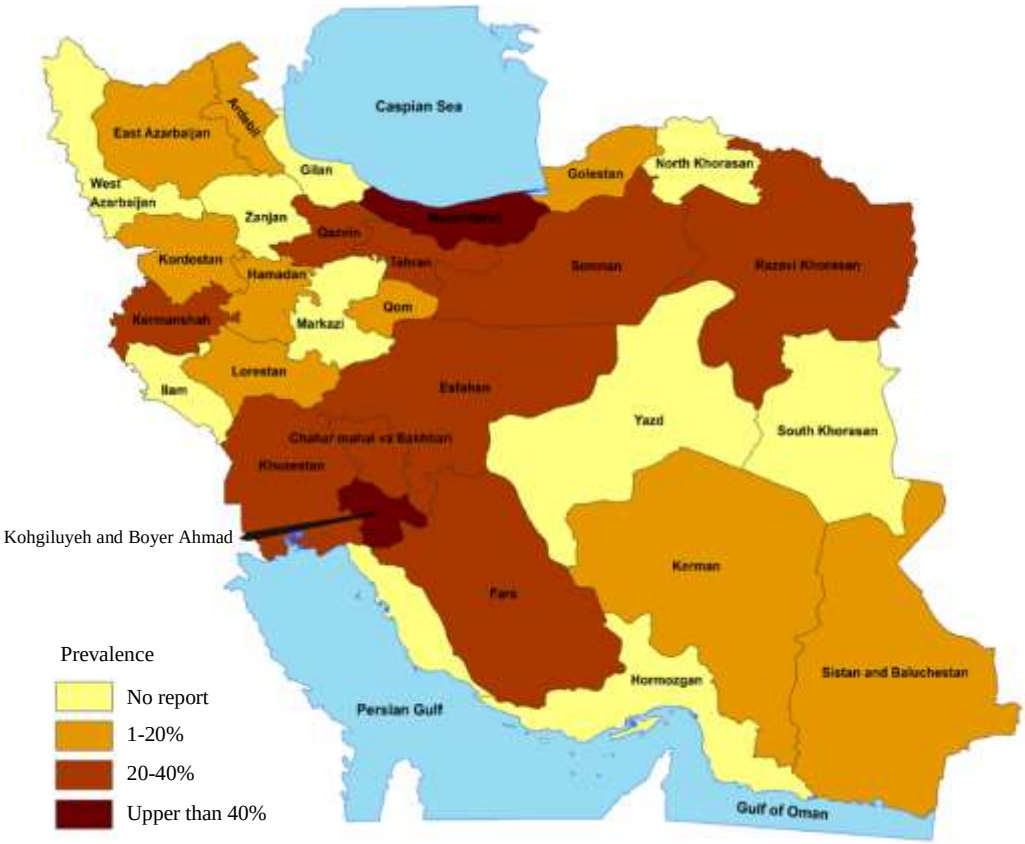

Fig. 4: Prevalence of neosporosis in cattle in different provinces of Iran

DOI: 10.3844/ajavsp.2021.23.38

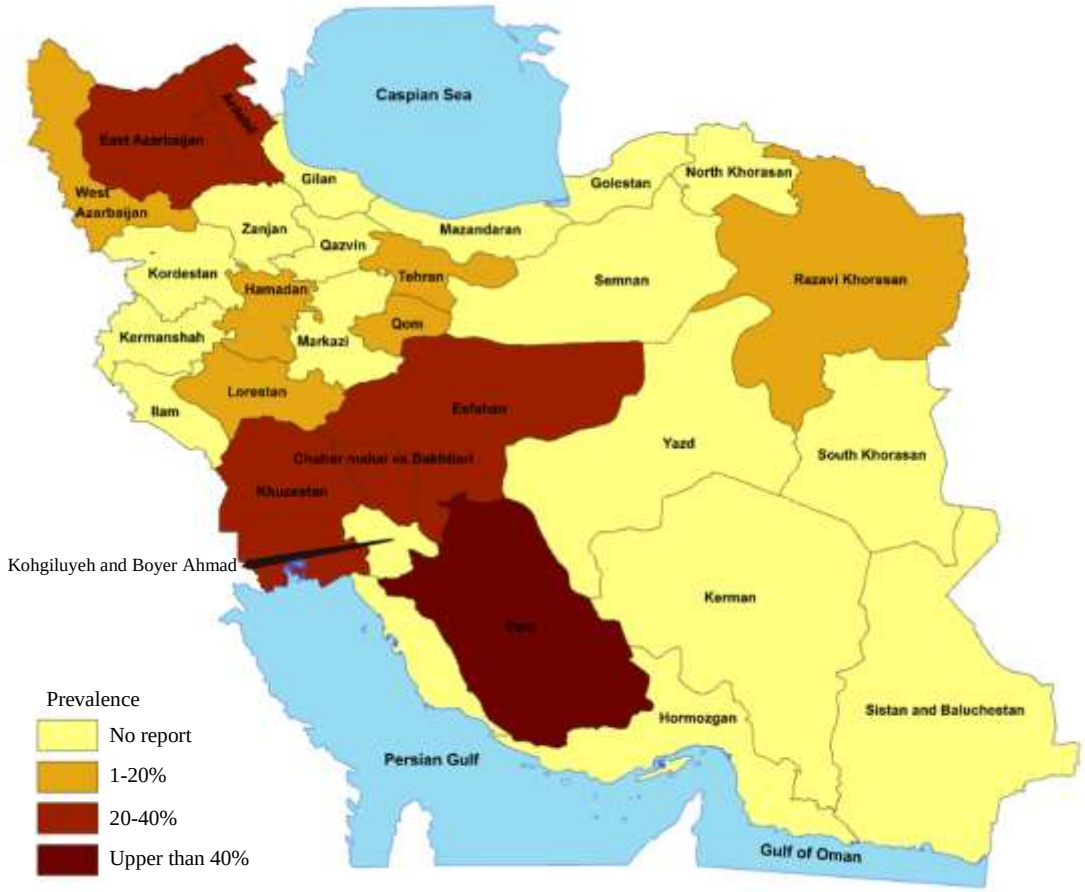

Fig. 5: Prevalence of neosporosis in dogs in different provinces of Iran

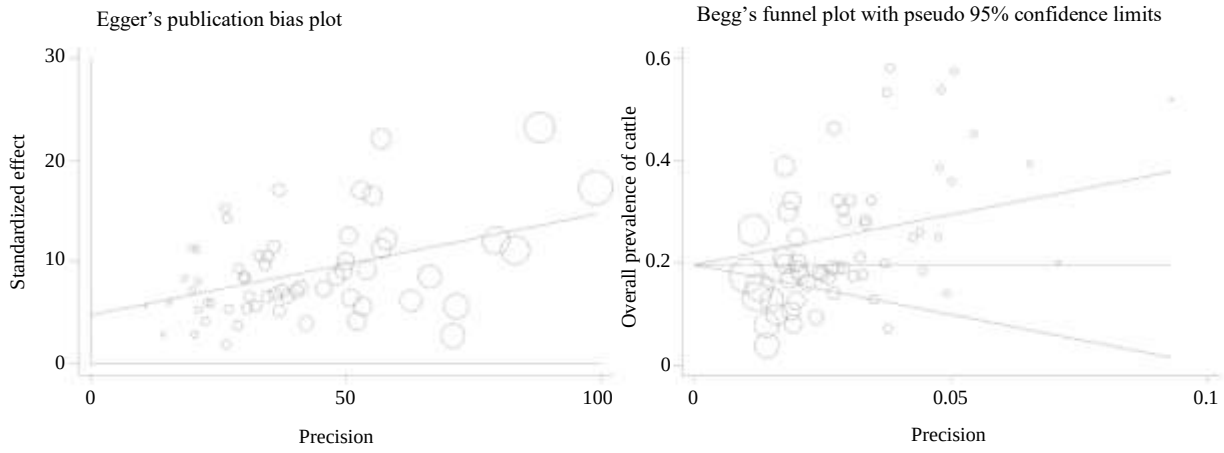

Fig. 6: Egger plot (a) and Begg's funnel plot with pseudo 95% confidence limits (b) for detection of publication bias in cattle

The overall prevalence of cattle and dog neosporosis in eight geographical regions of Iran is presented in Table 4. Also, a schematic image of neosporosis in cattle and dogs distribution was made based on studies conducted in the provinces of Iran (Fig. 4 and 5).

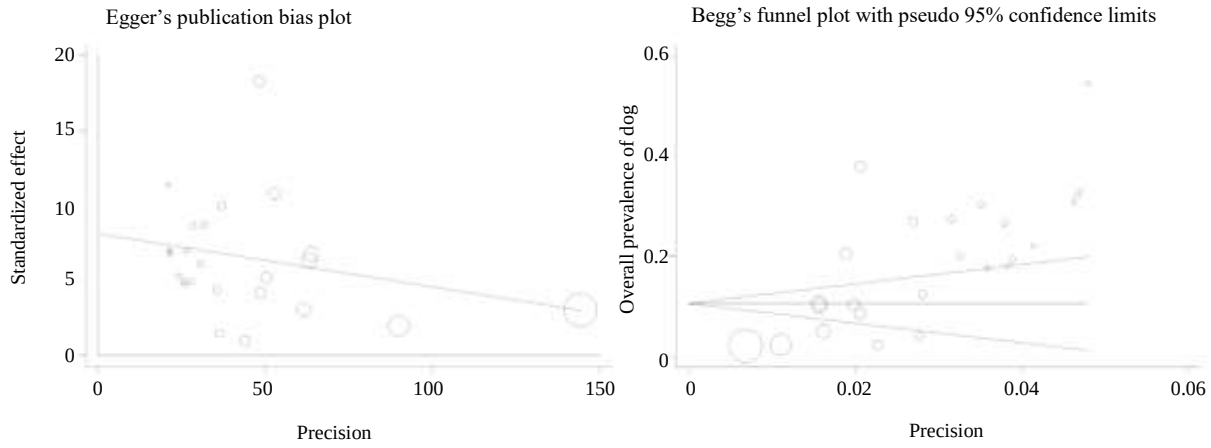

Fig. 7: Egger plot (a) and Begg's funnel plot with pseudo 95% confidence limits (b) for detection of publication bias in dogs

Publication Bias

Egger and Begg's tests were applied to check the presence of publication bias. The Begg's test (z = 3.62, p = 0.000 in cattle and z = 2.69, p = 0.007 in dogs) and the Egger test (bias = 4.75, 95%CI = 2.26-7.23 in cattle and bias = 8.11, 95%CI = 5.46-10.76 in dogs), indicating a significant publication bias of studies as shown in Fig. 6 and 7.

Discussion

The present study is the systematic review and meta-analysis that investigated both cattle and dog neosporosis, which is focused on Iran. This review was considered using 10 databases, 85 studies, 23,402 cattle and dogs and 2,862 positive cases. The present of this study showed that the overall prevalence of cattle neosporosis was 24.2% (95% CI, 21.5-26.9). The worldwide prevalence of *N. caninum* in cattle was estimated to be 20% (95% CI, 18-21), but our findings show an upper than to this range (Ribeiro *et al*., 2019). Despite, the mean prevalence of cattle neosporosis in the neighboring countries of Iran are as follows: In Turkey, two studies using the ELISA method in Central Anatolia, Kırşehir and Kars areas indicated that the prevalence were 13.96, 18.1 and 2%, respectively (Akca *et al*., 2005; Yıldız *et al*., 2017) and, in some Iraqi provinces, the overall prevalence of neosporosis was 17.5% (Mallah *et al*., 2012). Which are lower than the pooled prevalence in Iran. However, In Pakistan, two studies using the ELISA method in Punjab and Sindh provinces disclosed that the prevalence was 43.8 and 43%, respectively (Shabbir *et al*., 2011; Nazir *et al*., 2013). Which is higher than the pooled prevalence in Iran. If this high prevalence of bovine neosporosis is not controlled in Iran, it can lead to economic losses such as reproductive failure, expenses for professional help and diagnosis, lengthened intervals for rebreeding and culled cows' replacement, reduction of milk yield and reduced weight gain in infected animals (Trees *et al*., 1999; Ortega-Mora *et al*., 2006).

In the meta-analysis of subgroups, the highest prevalence of cattle neosporosis was estimated in Kohgiluyeh and Boyer-Ahmad province, in the southwest part of Iran as 51.7% and the lowest prevalence was found in Sistan and Baluchestan province, in the southeast of the country as 3.8%. There is a variation among the prevalence in each part of the country, which might be as a result of several causes such as the age, gender and Breeds of investigated animal, presence of an intermediate host, sampling and study methods, different years and various seasonal periods, farms management, food storage, contact with carnivores, distinct geographical regions and humid and temperate climate effect on viability and sporulation of *N. caninum* oocysts (Dubey *et al*., 2007; Atkinson *et al*., 2000).

The existence of dogs on the farm is a risk factor related to the seroprevalence of neosporosis in cattle (Moore and Venturini, 2018; Ribeiro *et al*., 2019) and close contact with rodents and poultry had a significant association with cattle neosporosis (Barling *et al*., 2001; Gharekhani and Yakhchali, 2019). Several investigations indicate that the eating of feed or water contaminated with *N. caninum* oocysts shed by dogs and ingesting of the aborted materials with carnivores played an important role in increasing horizontal transmission and postnatal infection in cattle (Malmasi *et al*., 2007; Haddadzadeh *et al*., 2007; McAllister, 2016). Furthermore, this study showed that the pooled prevalence of *N. caninum* infections between dogs in Iran was 19.9% (95% CI, 15.3-24.4). That compares to

the global rate (17.14%) Iran has a higher prevalence (Anvari *et al*., 2020). The mean prevalence of canine neosporosis in the neighboring countries of Iran is as follows: According to the worldwide meta-analysis study, the pooled prevalence in Turkey was 23.87% (Anvari *et al*., 2020) and in Pakistan, one study using the ELISA method disclosed that the seroprevalence was 23.5% (Nazir *et al*., 2014). Both prevalences are higher than the pooled prevalence in Iran.

In the meta-analysis of subgroups, the highest prevalence of neosporosis among dogs was estimated in Fars province, in the south part of Iran as 54.6% and the lowest prevalence was found in Lorestan province, in the west of the country as 2.1%. The reason for this wide variation is the existence of many risk factors associated with *N. caninum* infection, including Age, Gender, particular Breed, presence of an intermediate host, Type of living or feeding, coinfections and climate that could affect the transmission, sporulation and oocyst survival (Anvari *et al*., 2020; Collantes-Fernández *et al*., 2008; Reichel *et al*., 2007).

A study demonstrated that there is an association between climate and neosporosis frequency in Iran. *N. caninum* infection among cattle in cold climate regions is less than those in warm, dry and mild climate areas (Youssefi *et al*., 2010). In the current study, the prevalence was considerably high in Southwest of Iran, 37% in cattle and 30.6% in dogs, because it is located in warm, dry and mild climate areas compared to other parts of Iran. Furthermore, the prevalence in East Azerbaijan (15.4% in dogs), West Azerbaijan (16.8% in cattle) and Ardabil (7% in cattle) provinces, which are located in the northwest of Iran, was relatively low. This low rate may be due to the reality that all cold mentioned and mountainous regions are not in favor of oocyst sporulation and survival (Dubey *et al*., 2017).

Integrated control strategies and measures should be considered to prevent and control neosporosis in canines, which will have important implications for controlling neosporosis in intermediate hosts such as sheep, goats and cattle. The diet source of the animal plays a momentous role in the horizontal transmission and as well as for the completion of the *N. caninum* life cycle (Dubey *et al*., 2007). However, the existence of canine working may inhibit visits from other canids on the farm, decreasing the risk of neosporosis in cattle (Barling *et al*., 2001). The removal of seropositive animals with a history of abortion to decrease the infection rate and economic burden consequently was suggested (Ansari-Lari *et al*., 2017).

This study has its limitations; such an analysis is limited due to the heterogeneity among studies' results. Even though there are widespread research studies and a large number of these may have been done on this subject, but they have not been publicly available. The current meta-analysis excluded these theses. This can explain as one of the reasons for the publication bias in the present study.

Conclusion

In conclusion, the pooled prevalence of cattle and dogs neosporosis in Iran is relatively high at 24.2 and 19.9%, respectively. This value differs among geographical regions as it is the maximum in the Southwest for both and the minimum in Northeast for cattle and Southeast for dogs of Iran. These results are desirable for managing the control programs of this infection.

Furthermore, there is a clear gap in the prior studies, firstly there is no enough attention paid to the risk factors containing: The presence of dogs, age and breed of studied cattle and type of production system and the important role of them in the epidemiology of the disease. Secondly, there is no enough paid to the reproductive performance of seropositive cattle and subsequently their economic losses. Hence, all the above-mentioned parameters are required to consider to overcome these shortcomings in the future. An emphasis should be made prevention of the infection at the farm level by using procedures to test bulk milk, cattle and dogs.

Acknowledgment

The authors hereby would like to express their gratitude and appreciation to Dr. Mehran Farhoodi for collaboration and providing advice on the implementation of this meta-analysis in different stages and sections.

Authors' Contributions

Mohammad Jokar: Organized the study, proposal of study writing, data gathering, manuscript preparation, literature search and final revision of the study.

Saied Bokaie: Proposal of study writing, analysis and interpretation of data, manuscript editing, final revision of the study content, final approval of the revision the manuscript.

Vahid Rahmanian: Design of study, analysis and interpretation of data literature search and final revision of the study content, final approval of the version the manuscript.

Razieh Zahedi: Design of study, analysis and interpretation of data literature search and final revision of the study content, final approval of the version the manuscript.

Nader Sharifi and Hekmatollah Khoubfekr: Data gathering, manuscript editing, literature search and final revision of the study content, final approval of the version the manuscript.

Ethics in Systematic Reviews

The authors of this study followed the ethical principles of Systematic Reviews, including guidance on authorship, avoiding redundant (duplicate) publication, avoiding plagiarism, transparency, ensuring accuracy that potential complications.

Conflict of Interest

The authors declared that there are no conflicts of interest.

References

Adhami, G. H., Hoghooghi, R. N., & Dalimi, A. A. (2014). The SERO epidemiological investigation into *neospora caninum* in cattle in sanandaj, kordestan province.

Adhami, G., Dalimi, A., Ranjbar-Bahadori, S., & Morovati, H. (2015). Evaluation of *Neospora caninum* infection in industrial and traditional dairy farms of Sanandaj province by IFAT. J Large Anim Clin Res, 8(1), 53-62.

Ahmad, N., Jozani, J., & Neda, Z. (2011). Adaptation of Dot-Elisa for serodiagnosis of *Neospora caninum* infestation in aborted cows. Global Veterinaria, 7(2), 149-152.

Akca, A., Gokce, H. I., Guy, C. S., McGarry, J. W., & Williams, D. J. (2005). Prevalence of antibodies to *Neospora caninum* in local and imported cattle breeds in the Kars province of Turkey. Research in veterinary science, 78(2), 123-126.

Ansarifar, M. (2011). Investigation of the *neospora caninum* prevalence in livestock farms in Alborz province by ELISA, Master's Thesis, School of Veterinary Medicine, Islamic Azad University of Karaj Branch, Karaj, Iran. https://elmnet.ir

Ansari-Lari, M., Ahmadnia, S., Moraveji, M., Bahrami, S., & Hosseini, A. (2011). Seroepidemiological study of *Neospora caninum* in dairy cattle, Iran. Online J Vet Res, 15, 155-161.

Ansari-Lari, M., Rowshan-Ghasrodashti, A., Jesmani, H., Masoudian, M., & Badkoobeh, M. (2017). Association of *Neospora caninum* with reproductive performance in dairy cows: A prospective study from Iran. In Veterinary Research Forum (Vol. 8, No. 2, p. 109). Faculty of Veterinary Medicine, Urmia University, Urmia, Iran.

Anvari, D., Saberi, R., Sharif, M., Sarvi, S., Hosseini, S. A., Moosazadeh, M., ... & Daryani, A. (2020). Seroprevalence of *Neospora caninum* infection in dog population worldwide: A systematic review and meta-analysis. Acta Parasitologica, 1-18.

Asadi Karam, M. (2016). Serological Survey of *Neospora Caninum* Infection in Cattle in Shahr-e-Babak City, Master's Thesis, School of Veterinary Medicine, Shahrekord University, Shahrekord, Iran. https://irandoc.ac.ir

Atashgahi, S. (2015). Seroprevalence of *Neospora caninum* infection of dairy cows in neyshabor using ELISA method, Master's Thesis, School of Veterinary Medicine, Shahrekord University, Shahrekord, Iran. https://irandoc.ac.ir

Atkinson, R. A., Cook, R. W., Reddacliff, L. A., Rothwell, J., Broady, K. W., Harper, P. A. W., & Ellis, J. T. (2000). Seroprevalence of *Neospora caninum* infection following an abortion outbreak in a dairy cattle herd. Australian Veterinary Journal, 78(4), 262-266.

Barling, K. S., McNeill, J. W., Paschal, J. C., Mccollum Iii, F. T., Craig, T. M., Adams, L. G., & Thompson, J. A. (2001). Ranch-management factors associated with antibody seropositivity for *Neospora caninum* in consignments of beef calves in Texas, USA. Preventive Veterinary Medicine, 52(1), 53-61.

Behnaz, M. K. (2017). Development and evaluation of an in- house ELISA test for anti- *Neospora caninum* antibodies detection in in cattle, Master's Thesis, School of Veterinary Medicine, Shahid Chamran Ahvaz University, Ahvaz, Iran. https://irandoc.ac.ir

Binaee, M. (2017). Serological examination of *Neospora caninum* contamination in dairy cows of Semnan city, Master's Thesis, School of Veterinary Medicine, Semnan University, Semnan, Iran. https://irandoc.ac.ir

Chatziprodromidou, I. P., & Apostolou, T. (2018). Diagnostic accuracy of enzyme-linked immunosorbent assay (ELISA) and immunoblot (IB) for the detection of antibodies against *Neospora caninum* in milk from dairy cows. Epidemiology & Infection, 146(5), 577-583.

Cleophas, T. J., & Zwinderman, A. H. (2017). Meta-analysis and Random Effect Analysis. In Modern Meta-Analysis (pp. 51-62). Springer, Cham.

Coelho, A. M., Cherubini, G., De Stefani, A., Negrin, A., Gutierrez-Quintana, R., Bersan, E., & Guevar, J. (2019). Serological prevalence of toxoplasmosis and neosporosis in dogs diagnosed with suspected meningoencephalitis in the UK. Journal of Small Animal Practice, 60(1), 44-50.

Collantes-Fernández, E., Gómez-Bautista, M., Miró, G., Álvarez-García, G., Pereira-Bueno, J., Frisuelos, C., & Ortega-Mora, L. M. (2008). Seroprevalence and risk factors associated with *Neospora caninum* infection in different dog populations in Spain. Veterinary Parasitology, 152(1-2), 148-151.

Curtis, B., Harris, A., Ullal, T., Schaffer, P. A., & Munoz Gutierrez, J. (2020). Disseminated *Neospora caninum* infection in a dog with severe colitis. Journal of Veterinary Diagnostic Investigation, 32(6), 923-927.

Davasaz, A. (2009). Seroprevalence of *Neospora caninum* in dairy farms of Tabriz region. In: 1th National Congress of Veterinary Laboratory Sciences, pp. 211-212. https://civilica.com

de Aquino Diniz, L. V., Minutti, A. F., Nino, B. D. S. L., Costa, L. R., Bosculo, M. R. M., de Almeida, B. F. M., ... & de Barros, L. D. (2019). Vertical transmission of *Neospora caninum* in bovine fetuses from a slaughterhouse in Brazil. Tropical animal health and production, 51(6), 1751-1755.

de Oliveira, F. C. R., Gallo, S. S. M., Bôa-Morte, M. D. O., & Ederli, N. B. (2019). Association of reproductive problems and dairy cow productivity in a farm with an outbreak of neosporosis abortion in Brazil. Am J Anim Vet Sci., 14: 7-12.

Decôme, M., Martin, E., Bau-Gaudreault, L., & O'Toole, E. (2019). Systemic disseminated *Neospora caninum* infection with cutaneous lesions as the initial clinical presentation in a dog. The Canadian veterinary journal= La revue veterinaire canadienne, 60(11), 1177-1181.

Demir, P. A., Eşki, F., & Ütük, A. E. (2020). Estimating the total economic costs of *Neospora caninum* infections in dairy cows in Turkey. Tropical Animal Health and Production, 52(6), 3251-3258.

DerSimonian, R., & Laird, N. (2015). Meta-analysis in clinical trials revisited. Contemporary clinical trials, 45, 139-145.

Didiano, A., Monti, P., Taeymans, O., & Cherubini, G. B. (2020). Canine central nervous system neosporosis: clinical, laboratory and diagnostic imaging findings in six dogs. Veterinary Record Case Reports, 8(1), e000905.

Dubey, J. P., Hemphill, A., Calero-Bernal, R., & Schares, G. (2017). Neosporosis in animals. CRC Press.

Dubey, J. P., Schares, G., & Ortega-Mora, L. M. (2007). Epidemiology and control of neosporosis and *Neospora caninum*. Clinical microbiology reviews, 20(2), 323-367.

Dwinata, I. M., Oka, I. B. M., Agustina, K. K., & Damriyasa, I. M. (2018). Seroprevalence of *Neospora caninum* in local Bali dog. Veterinary world, 11(7), 926.

Fard, S. R. N., Khalili, M., & Aminzadeh, A. (2008). Prevalence of antibodies to *Neospora caninum* in cattle in Kerman province, South East Iran. Veterinarski Arhiv, 78(3), 253.

Fereig, R. M., & Nishikawa, Y. (2020). From Signaling Pathways to Distinct Immune Responses: Key Factors for Establishing or Combating *Neospora caninum* Infection in Different Susceptible Hosts. Pathogens, 9(5), 384.

Forooghi, P. M. (2013). Serologic prevalence of infection with *Neospora caninum* in dairy cattle in Shahrekord by ELISA, Master's Thesis, School of Veterinary Medicine, Shahrekord University, Shahrekord, Iran. https://irandoc.ac.ir

Ghafarifar, F., Sabevarinejad, G., Dalimi, A., & Forouzandeh-Moghadam, M. (2014). Molecular detection of *Neospora caninum* from naturally infected dogs in Lorestan province, West of Iran. Archives of Razi Institute, 69(2), 185-190.

Ghahvei, Y. (2014). Serological survey do Neosporacaninum infection in cattle in Kermanshah, Master's Thesis. School of Veterinary Medicine, Shahid Bahonar University, Kerman, Iran. https://irandoc.ac.ir

Ghanavati, S. (2015). Investigation of serological and molecular prevalence of *Neospora caninum* parasite in Ahvaz city dogs, Master's Thesis, School of Veterinary Medicine, Shahid Chamran Ahvaz University, Ahvaz, Iran. https://irandoc.ac.ir

Gharekhani, J., & Heidari, H. (2014). Serology based comprehensive study of Neospora infection in domestic animals in Hamedan province, Iran. Journal of Advanced Veterinary and Animal Research, 1(3), 119-124.

Gharekhani, J., & Tavoosidana, G. (2013). Serological survey of *Neospora caninum* (Sarcocystidae) infection in beef cattle from western Iran. Scientia Parasitologica, 14(2), 95-98.

Gharekhani, J., & Yakhchali, M. (2019). *Neospora caninum* infection in dairy farms with history of abortion in west of Iran. Veterinary and Animal Science, 8, 100071.

Gharekhani, J., Haddadzadeh, H., & Bahonar, A. (2014a). Prevalence of immunoglobulin G (IgG) antibody to *Neospora caninum* in dairy cattle of Hamedan province, west of Iran. In Veterinary Research Forum: an International Quarterly Journal (Vol. 5, No. 2, p. 149). Faculty of Veterinary Medicine, Urmia University, Urmia, Iran.

Gharekhani, J., Tavoosidana, G., & Akbarein, H. (2014b). Serological study of *Neospora caninum* infection in dogs and cattle from west of Iran. Comparative Clinical Pathology, 23(5), 1203-1207.

Gharekhani, J., Heidari, H., & Akbarein, H. (2012). Seroepidemiology of *Neospora caninum* in Iranian native and crossbreed cattle: across sectional study. Journal of Veterinary Research, 67(4), 325-329.

Gharekhani, J., Yakhchali, M., Abbasi-Doulatshahi, E., & Barati, E. (2019). Seroprevalence of *Neospora caninum* and Toxoplasma gondii infections in stray dogs of Hamadan suburb, west of Iran, 2018. Avicenna Journal of Clinical Microbiology and Infection, 6(2), 57-60.

González-Warleta, M., Castro-Hermida, J. A., Calvo, C., Pérez, V., Gutiérrez-Expósito, D., Regidor-Cerrillo, J., ... & Mezo, M. (2018). Endogenous transplacental transmission of *Neospora caninum* during successive pregnancies across three generations of naturally infected sheep. Veterinary research, 49(1), 106.

Hadad Zadeh, H. R., Shayan, P., Vojgani, M., & Bolorchi, M. (2010). Serological study of *Neospora caninum* in pregnant dairy cattle in Tehran, Iran. Iranian Journal of Veterinary Medicine, 4(2).

Haddadzadeh, H. R., Sadrebazzaz, A., Malmasi, A., Ardakani, H. T., Nia, P. K., & Sadreshirazi, N. (2007). Seroprevalence of *Neospora caninum* infection in dogs from rural and urban environments in Tehran, Iran. Parasitology research, 101(6), 1563-1565.

Haji Hajikolaei, M. R., Hamidinejat, H., Ghorbanpoor, M., & Goraninejad, S. (2008). Serological study of *Neospora caninum* infection in cattle from Ahvaz area, Iran. Iranian Journal of Veterinary Medicine, 2(2), 63-66.

Hamidinejat, H., Hajikolaei, M. R. H., Ghorbanpoor, M., Namavari, M., & Gol, S. M. A. (2013). Development and Standardization of Dot–ELISA for Detection of *Neospora caninum* Antibodies in Cattle and Comparison with Standard Indirect ELISA and Direct Agglutination Test (DAT). Iranian journal of parasitology, 8(4), 634.

Hamidinejat, H., Shapouri, M. R. S. A., Namavari, M. M., Shayan, P., & Kefayat, M. (2015). Development of an indirect ELISA using different fragments of recombinant Ncgra7 for detection of *Neospora caninum* infection in cattle and water buffalo. Iranian Journal of Parasitology, 10(1), 69.

Hatami, S. (2014). Evaluation of production and reproduction data of a dairy farm after serological test for BLV, IBR, Johne's disease and Neosporosis, Master's Thesis, School of Veterinary Medicine, Ferdowsi University Mashhad, Mashhad, Iran. https://irandoc.ac.ir

Heidari, H., Mohammadzadeh, A., & Gharekhani, J. (2014). Seroprevalence of *Neospora caninum* in slaughtered native cattle in Kurdistan province, Iran. In Veterinary research forum: an international quarterly journal (Vol. 5, No. 1, p. 69). Faculty of Veterinary Medicine, Urmia University, Urmia, Iran.

Hosseininejad, M., & Hosseini, F. (2011). Seroprevalence of *Neospora caninum* and Toxoplasma gondii infection in dogs from west and central parts of Iran using two indirect ELISA tests and assessment of associate risk factors. Iranian Journal of Veterinary Research, 12(1), 46-51.

Hosseininejad, M., & Hosseini, F. (2019). Seroprevalence of *Neospora caninum* and Toxoplasma gondii in dogs in Ahwaz, Iran.

Hosseininejad, M., Hosseini, F., Mosharraf, M., Shahbaz, S., Mahzounieh, M., & Schares, G. (2010a). Development of an indirect ELISA test using an affinity purified surface antigen (P38) for sero-diagnosis of canine *Neospora caninum* infection. Veterinary parasitology, 171(3-4), 337-342.

Hosseininejad, M., Hosseini, F., Mahzounieh, M., Nafchi, A. R., & Mosharraf, M. (2010b). Seroprevalence of *Neospora caninum* infection in dogs in Chaharmahal-va-Bakhtiari Province, Iran. Comparative clinical pathology, 19(3), 269-270.

Hosseininejad, M., Mahzounieh, M., & Esfandabadi, N. S. (2017). *Neospora caninum* suspects as one of the most important causes of abortion in large dairy farms in Isfahan, Iran. Iranian Journal of Parasitology, 12(3), 408.

Javanshir, A. (2015). Prevalence of *Neospora caninum* parasitic infection in dairy cattle and guard dogs in Qom Lebanon Complex using ELISA, Master's Thesis, School of Veterinary Medicine, Shahrekord University, Shahrekord, Iran. https://irandoc.ac.ir

Jin, X., Li, G., Zhang, X., Gong, P., Yu, Y., & Li, J. (2017). Activation of a *Neospora caninum* EGFR-like kinase facilitates intracellular parasite proliferation. Frontiers in microbiology, 8, 1980.

Jokar, M., Amanatchi, A., Baghdadi, M., & Nadia, T. (2018). Investigation of the simultaneous presence of *Neospora caninum* antigen and antibody in dairy cows in the suburbs of Qom province. In: 12th Congress of Iranian Veterinary Students, pp. 86-87. https://civilica.com

Kamkar-Salehi, S., & Namavari, M. (2017). Study of using the triple Dot-ELISA for simultaneous diagnosis of *Neospora caninum*, IBR and BVDV. Vet Res Biol Prod, 30(4), 134-140.

Keyhani, P. (2017). Molecular study of *Neospora caninum* infection in dogs of Isfahan province.

Khan, A., Shaik, J. S., Sikorski, P., Dubey, J. P., & Grigg, M. E. (2020). Neosporosis: An Overview of Its Molecular Epidemiology and Pathogenesis. Engineering, 6(1), 10-19.

Khanmohammadi, M., & Fallah, E. (2011). Prevalence of *Neospora caninum* antibodies in shepherd dogs in Sarab district, East Azerbaijan province, Iran. African Journal of Microbiology Research, 5(28), 5062-5066.

Khordadmehr, M., Hosseini, S., Mohsenifar, E., Namavari, M., & Khordadmehr, S. (2012). Seroprevalence of Neospora caninum in farm and household dogs determined by ELISA. Online J Vet Res, 16(4), 172-81.

Klein, C., Barua, S., Liccioli, S., & Massolo, A. (2019). *Neospora caninum* DNA in coyote fecal samples collected in an urban environment. Journal of wildlife diseases, 55(1), 196-199.

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P., ... & Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Journal of clinical epidemiology, 62(10), e1-e34.

Liu, Y., Reichel, M. P., & Lo, W. C. (2020). Combined control evaluation for *Neospora caninum* infection in dairy: Economic point of view coupled with population dynamics. Veterinary Parasitology, 277, 108967.

Mallah, M. O., Dawood, K. A., & Alrodhan, M. A. (2012). Seroepidemiological study for the prevalence of *Neospora caninum* in Dairy & Beef cattle in some Iraqi provinces. Al-Qadisiyah Journal of Veterinary Medicine Sciences, 11(1), 103-110.

Malmasi, A., Hosseininejad, M., Haddadzadeh, H., Badii, A., & Bahonar, A. (2007). Serologic study of anti-*Neospora caninum* antibodies in household dogs and dogs living in dairy and beef cattle farms in Tehran, Iran. Parasitology Research, 100(5), 1143-1145.

Marugan-Hernandez, V. (2017). *Neospora caninum* and bovine neosporosis: current vaccine research. Journal of comparative pathology, 157(2-3), 193-200.

McAllister, M. M. (2016). Diagnosis and control of bovine neosporosis. Veterinary Clinics: Food Animal Practice, 32(2), 443-463.

Mohammad Ali Gol, S. (2010). Development of Dot-ELISA for diagnosis of *Neospora caninum* infection in cattle and Evaluation with Elisa Kit, Master's Thesis, School of Veterinary Medicine, Shahid Chamran Ahvaz University, Ahvaz, Iran. https://irandoc.ac.ir

Moore, D. P., & Venturini, M. C. (2018). Neospora. In Parasitic Protozoa of Farm Animals and Pets (pp. 125-148). Springer, Cham.

Moraveji, M. (2012). Production of recombinant *neospora caninum* ncsag1 antigen for applying in setting of latex agglutination test (lat) and its comparison to the commercial elisa kit, Master's Thesis, School of Veterinary Medicine, Shiraz University, Shiraz, Iran. https://irandoc.ac.ir

Morovati, H., & Noaman, V. (2016). Seroepidemiology of *Neospora Caninum* in Dairy Cattle Farms with a History of Abortion in Isfahan Province. Iran. J Vet Sci Anim Husb, 4(3), 304.

Motamedi Pour, S. (2016). Seroprevalence of *Neospora caninum* in lactating cattle of Sirjan peovince, Master's Thesis, School of Veterinary Medicine, Shahrekord University, Shahrekord, Iran. https://irandoc.ac.ir

Namavari, M., Hosseini, M. H., Mansourian, M., Shams, Z., Amrabadi, O., Tahamtan, Y., & Moazeni-Jula, F. (2012). Testing for infective abortive agents in cattle in Iran. Online Journal of Veterinary Research, 16(3), 147-153.

Nayebzadeh, H., Nourollahi Fard, S. R., Khalili, M., Zakian, N., & Taati, M. (2015). Seroprevalence of *Neospora caninum* infection in dairy cattle in west of Iran. Acta Vet Eurasia, 41(2), 162–166.

Nazir, M. M., Maqbool, A., Akhtar, M., Ayaz, M., Ahmad, A. N., Ashraf, K., ... & Lindsay, D. S. (2014). *Neospora caninum* prevalence in dogs raised under different living conditions. Veterinary Parasitology, 204(3-4), 364-368.

Nazir, M. M., Maqbool, A., Khan, M. S., Sajjid, A., & Lindsay, D. S. (2013). Effects of age and breed on the prevalence of *Neospora caninum* in commercial dairy cattle from Pakistan. The Journal of parasitology, 99(2), 368-370.

Nemat, E. A., & Jafari, J. R. (2010). Study on pattern of *Neospora caninum* tachyzoite proteins by SDS-PAGE and Western blotting in aborted cows.

Nematollahi, A., Jaafari, R., & Moghaddam, G. (2011a). Seroprevalence of *Neospora caninum* infection in dairy cattle in Tabriz, Northwest Iran. Iranian Journal of Parasitology, 6(4), 95.

Nematollahi, A., Jafari, R., & Moghaddam, G. (2011b). The study of infestation to *Neospora caninum* using the standardized domestic ELISA in dairy cows in suburb of Tabriz. Iran Vet J, 7(30), 57, [Persian]. https://magiran.com

Nematollahi, A., Moghaddam, G. H., Jaafari, R., Helan, J. A., & Norouzi, M. (2013). Study on outbreak of *Neospora caninum*-associated abortion in dairy cows in Tabriz (Northwest Iran) by serological, molecular and histopathologic methods. Asian Pacific journal of tropical medicine, 6(12), 942-946.

Noaman, V., & Nabinejad, A. R. (2020). Seroprevalence and risk factors assessment of the three main infectious agents associated with abortion in dairy cattle in Isfahan province, Iran. Tropical Animal Health and Production, 1-9.

Noori, M., Rasekh, M., Ganjali, M., & FARD, S. R. N. (2019). Seroprevalence of *Neospora caninum* Infection and Associated Risk Factors in Cattle of Sistan Areas, Southeastern Iran in 2016. Iranian journal of parasitology, 14(2), 340.

Nourollahi-Fard, S. R., Khalili, M., Fazli, O., Sharifi, H., & Radfar, M. H. (2017). Seroprevalence of *Neospora caninum* in cattle of Neishabour, northeast Iran. Slovenian Veterinary Research, 54(1), 5-9.

Ortega-Mora, L. M., Fernández-García, A., & Gómez-Bautista, M. (2006). Diagnosis of bovine neosporosis: recent advances and perspectives. Acta Parasitologica, 51(1), 1-14.

Pazoki Plasht, T., Rabie Far, O., Mohammad Sadegh, M., & Gomashchi, H. (2008). Contamination of animals with a history of abortion with Brucella abortus, BVD, IBR and *Neospora caninum*. 15th Iranian Veterinary Congress, pp. 111-112. https://civilica.com

Pouramini, A., Jamshidi, S., Shayan, P., Ebrahimzadeh, E., Namavari, M., & Shirian, S. (2017). Molecular and serological detection of *Neospora caninum* in multiple tissues and CSF in asymptomatic infected stray dogs. Iranian Journal of Veterinary Medicine, 11(2), 105-112.

Raeisi, A. (2009). Seroprevalence of *Neospora caninum* infection in dogs of Chaharmahal and Bakhtiari province using indirect antibody test. http://ganj-old.irandoc.ac.ir/articles/511596

Ranjbar, B. S., Motevaselian, A. H., Bokaie, S., & Yousefi, M. (2010). Serological study of *Neospora caninum* in aborted dairy cattle in Garmsar.

Razmi, G. (2009). Fecal and molecular survey of *Neospora caninum* in farm and household dogs in Mashhad area, Khorasan province, Iran. The Korean journal of parasitology, 47(4), 417.

Razmi, G. R., Mohammadi, G. R., Garrosi, T., Farzaneh, N., Fallah, A. H., & Maleki, M. O. H. S. E. N. (2006). Seroepidemiology of *Neospora caninum* infection in dairy cattle herds in Mashhad area, Iran. Veterinary Parasitology, 135(2), 187-189.

Razmi, G., Zarae, H., Norbakhsh, M. F., & Naseri, Z. (2014). Estimating the rate of transplacental transmission of *Neospora caninum* to aborted fetuses in seropositive dams in Mashhad area, Iran. Iranian Journal of Veterinary Medicine, 7(4), 253-256.

Reichel, M. P., Ellis, J. T., & Dubey, J. P. (2007). Neosporosis and hammondiosis in dogs. Journal of Small Animal Practice, 48(6), 308-312.

Reichel, M. P., Wahl, L. C., & Ellis, J. T. (2020). Research into *Neospora caninum*—what have we learnt in the last thirty years?. Pathogens, 9(6), 505.

Ribeiro, C. M., Soares, I. R., Mendes, R. G., de Santis Bastos, P. A., Katagiri, S., Zavilenski, R. B., ... & Afreixo, V. (2019). Meta-analysis of the prevalence and risk factors associated with bovine neosporosis. Tropical animal health and production, 1-18.

Rocchigiani, G., Poli, A., Nardoni, S., Papini, R., & Mancianti, F. (2017). *Neospora caninum* in wild waterfowl: occurrence of parasite DNA and low antibody titers. Journal of Parasitology, 103(1), 142-145.

Ruppar, T. (2020). Meta-analysis: How to quantify and explain heterogeneity?. European Journal of Cardiovascular Nursing, 19(7), 646-652.

Saber, E., Jafari, R., & Ahmad, N. (2010). Comparison results of a domestic indirect ELISA for detection of antibodies Toxoplasma Gondeii to the results of a commercial ELISA for detection of antibodies Neospora Caninum, Iranian Journal of Veterinary Clinical Sciences, 4(1), 33. magiran.com/p1081512

Sabevarinejad, G. H. A., Dalimi, A., Ghafarifar, F., & Forouzandeh-Moghadam, M. (2013). Serological survey of *Neospora caninum* infection in Holstein dairy cattle from Khoramabad region. Vet Res Biol Prod, 26(4), 48-54.

Sadrebazzaz, A., Haddadzadeh, H., Esmailnia, K., Habibi, G., Vojgani, M., & Hashemifesharaki, R. (2004). Serological prevalence of *Neospora caninum* in healthy and aborted dairy cattle in Mashhad, Iran. Veterinary Parasitology, 124(3-4), 201-204.

Sattari, A., Moshiri, F., & Musavi, S. (2011). The seroprevalence of *Neospora caninum* antibodies in dairy cattle herds in Golestan province, Iran. J Vet Microbiol, 7(1), 60-64.

Shabani, H., Rahimi, F., Fatahi, S., & Angoti, M. (2017). Seroepidemiology investigation of cattle neosporosis in Qazvin city. 11th Iranian Congress of Veterinary Students, pp. 90–91. https://civilica.com

Shabbir, M. Z., Nazir, M. M., Maqbool, A., Lateef, M., Shabbir, M. A. B., Ahmad, A., ... & Ijaz, M. (2011). Seroprevalence of *Neospora caninum* and Brucella abortus in dairy cattle herds with high abortion rates. Journal of Parasitology, 97(4), 740-742.

Shahidi, M., (2018). A study of neosporian abortion and congenital transmission in dairy farms of Torbat-E Heydariyeh area, Master's Thesis, School of Veterinary Medicine, Ferdowsi University Mashhad, Mashhad, Iran. https://irandoc.ac.ir

Sharifdini, M., Mohebali, M. E. H. D. I., Keshavarz, H., Hosseininejad, M., Hajjaran, H., Akhoundi, B., ... & Charehdar, S. (2011). *Neospora caninum* and Leishmania infantum co-infection in domestic dogs (Canis familiaris) in Meshkin-Shahr district, Northwestern Iran. Iranian journal of arthropod-borne diseases, 5(2), 60.

Silva, R. C., & Machado, G. P. (2016). Canine neosporosis: perspectives on pathogenesis and management. Veterinary Medicine: Research and Reports, 7, 59.

Tavanaee, H. R., & Namavari, M. (2017). Evaluation of attenuated variety of *Neospora caninum* for diagnosis of infection in cattle by agglutination test. Veterinary Researches & Biological Products, 30(2), 153-157.

Tavasolian, A. H., Ranjbar-Bahadori, S., & Youssefi, M. R. (2010). Seroepidemiology investigation of cattle neosporosis in garmsar city. 16th Iranian Veterinary Congress, pp. 78-79, (retrieved from https://civilica.com).

Trees, A. J., Davison, H. C., Innes, E. A., & Wastling, J. M. (1999). Towards evaluating the economic impact of bovine neosporosis. International journal for parasitology, 29(8), 1195-1200.

Yagoob, G. (2012a). Seroepidemiology of *Neospora caninum* in cattle in East-Azerbaijan province, North West Iran. Journal of Animal and Veterinary Advances, 11(5), 645-648.

Yagoob, G. (2012b). Seroprevalence of *Neospora caninum* in Stray Dogs of Tabriz, Iran. Journal of Animal and Veterinary Advances, 11(6), 723-726.

Yakhchali, M., Bahrami, M., Asri-Rezaei, S., & Bokaie, S. (2017). The enzymes and electrolytes profiles in sera of Iranian stray dogs naturally infected with *Neospora caninum*. Annals Ann Parasitol, 63(1), 63-68.

Yakhchali, M., Javadi, S., & Morshedi, A. (2010). Prevalence of antibodies to *Neospora caninum* in stray dogs of Urmia, Iran. Parasitology research, 106(6), 1455-1458.

Yıldız, K., Gökpınar, S., Sürsal, N., & Değirmenci, R. (2017). Seroprevalence of *Neospora caninum* in Dairy Cattle Raised in Çiçekdağı District of Kırşehir Province. Turkiye parazitolojii dergisi, 41(3), 135-138.

Yousefi, M. R., ARAB, K. F., & TABAR, M. H. A. (2009). Seroprevalence of *Neospora caninum* infection in rural and industrial cattle in northern Iran.

Youssefi, M. R., Ebrahimpour, S., & Esfandiari, B. (2010). Survey of *Neospora caninum* antibody in aborting cattle from three climate regions of Iran. World Applied Science Journal, 10, 1448-1451.