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

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**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, Elmnnet, Magiran, Irandoc, Iranmedex, Scientific Information Database (SID) and culicila. In cattle, 57 studies and in dogs 28 studies reporting the prevalence 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, deer 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., PubMed, Google Scholar, Science Direct, Scopus, Web of Science and five Persian databases namely, Elmet, 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 (%) |
|--------------------------|---------------------|------------------|---------------|-----------------|---------------|-------------|-------------------------|------------------------|
| Hosseiminejad et al.     | 2017                | Center           | Isfahan       | ELISA           | Sn ≥ 0.153    | 1500        | 395                     | 26.33                  |
| Nourollahi-Fard et al.   | 2017                | Northeast        | Razavi Khorasan | ELISA           | PP ≥ 0.2      | 100         | 26                      | 26.00                  |
| Morovati and Noaman      | 2016                | Center           | Isfahan       | ELISA           | S/P ≥ 0.5     | 611         | 196                     | 32.10                  |
| Gharekhani et al.        | 2014                | 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 ≥ 0.2      | 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 ≥ 0.4     | 1406        | 245                     | 17.40                  |
| Sattari et al.           | 2011                | Northwest        | Golestan      | ELISA           | S/P ≥ 0.5     | 800         | 107                     | 13.37                  |
| Nematomilash et al.      | 2011a               | Northwest        | East Azerbaijan | ELISA           | Sn ≥ 0.153    | 266         | 28                      | 10.50                  |
| Hamidinejat et al.       | 2013                | South            | Fars          | ELISA           | S/P ≥ 0.5     | 178         | 95                      | 53.30                  |
| Haji Hajoieki 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 Yakbarzani| 2019                | West             | Hamedan       | ELISA           | S/P ≥ 0.5     | 476         | 118                     | 24.80                  |
| Nematomilash et al.      | 2011b               | Northwest        | East Azerbaijan | ELISA           | S/P ≥ 0.3     | 76          | 13                      | 18.40                  |
| Adhami et al.            | 2014                | West             | Kurdistan     | ELISA           | S/P ≥ 0.5     | 336         | 64                      | 17.60                  |
| Ranjab et al.            | 2010                | North            | Semnan        | ELISA           | S/P ≥ 0.5     | 104         | 40                      | 38.50                  |
| Location | Year | Region | Assay | Titration | Positive | Negative | Comparison |
|----------|------|--------|-------|-----------|----------|----------|------------|
| West Hamedan | 2012 | West | ELISA | S/P ≥ 0.5 | 400 | 80 | 20.00 |
| West Lorestan | 2013 | West | ELISA | S/P ≥ 0.5 | 181 | 50 | 27.62 |
| West Kurdistan | 2015 | West | IFA | 1:200 | 410 | 69 | 16.82 |
| South Fars | 2017 | South | ELISA | S/P ≥ 0.5 | 184 | 59 | 32.07 |
| Qom | 2015 | North East | ELISA | S/P ≥ 0.5 | 200 | 18 | 8.00 |
| Kerman | 2016 | South East | ELISA | S/P ≥ 0.5 | 250 | 45 | 18.00 |
| Lorestan | 2013 | West | ELISA | S/P ≥ 0.5 | 184 | 52 | 28.26 |
| Kermanshah | 2014 | West | ELISA | S/P ≥ 0.5 | 92 | 33 | 35.86 |
| South Kerman | 2015 | East | ELISA | S/P ≥ 0.5 | 150 | 14 | 9.30 |
| Qazvin | 2017 | North West | ELISA | S/P ≥ 0.5 | 160 | 40 | 21.00 |
| Tehran | 2011 | North | ELISA | S/P ≥ 0.5 | 210 | 35 | 17.00 |
| Ardebil, Semnan | 2010 | North West | ELISA | S/P ≥ 0.5 | 46 | 3 | 7.00 |
| Razavi Khorasan | 2014 | North East | ELISA | S/P ≥ 0.5 | 200 | 38 | 19.00 |
| Fars, Kohgiluyeh and Boyer-Ahmad | 2012 | South West | ELISA | S/P ≥ 0.5 | 56 | 22 | 39.28 |
| East Azerbaijan | 2010 | North East | ELISA | S/P ≥ 0.5 | 136 | 24 | 17.60 |
| East Azerbaijan | 2011 | North East | ELISA | S/P ≥ 0.5 | 32 | 7 | 20.00 |
| East Azerbaijan | 2010 | North East | IgG | 116 | | 23.00 |
| East Azerbaijan | 2013 | North East | IgG | 76 | | 14.00 |
| Tehran | 2008 | North | ELISA | S/P ≥ 0.5 | 150 | 26 | 17.33 |
| Khuzestan | 2015 | South West | ELISA | S/P ≥ 0.5 | 108 | 58 | 53.70 |
| Semnan | 2017 | North | ELISA | S/P ≥ 0.5 | 237 | 67 | 28.27 |
| Fars | 2012 | South | ELISA | S/P ≥ 0.5 | 164 | 23 | 14.00 |
| Razavi Khorasan | 2018 | Northeast | ELISA | S/P ≥ 0.5 | 280 | 45 | 16.08 |
| Khuzestan | 2016 | Southwest | ELISA | S/P ≥ 0.5 | 280 | 87 | 32.07 |
| Razavi Khorasan | 2010 | Northeast | ELISA | S/P ≥ 0.5 | 178 | 95 | 53.30 |
| Razavi Khorasan | 2014 | Northeast | ELISA | S/P ≥ 0.5 | 638 | 190 | 29.90 |
| Tehran | 2007 | North | IFAT | 1:50 | 100 | 33 | 33.00 |
| West Azerbaijan | 2010 | Northwest | IFAT | 1:50 | 135 | 36 | 26.60 |
| Ardabil | 2011 | Northwest | ELISA | S/I ≥ 0.23 | 171 | 52 | 30.40 |
| Hamedan | 2013 | West | ELISA | S/P ≥ 0.40 | 270 | 73 | 27.00 |
| Hamedan | 2010 | West | IFAT | 1:50 | 100 | 31 | 31.00 |
| Khuzestan | 2015 | Southwest | IFAT | 1:50 | 150 | 30 | 20.00 |
| Semnan | 2017 | Center | ELISA | S/I ≥ 0.5 | 42 | 1 | 2.22 |
| Tehran | 2011 | Center | IFAT | 1:50 | 384 | 41 | 10.60 |
| Hamedan | 2014 | West | IFAT | 1:50 | 270 | 70 | 27.00 |
| Tehran | 2007 | North | IFAT | 1:50 | 103 | 20 | 19.40 |
| Chahar Mahal and Bakhhtiari, Isfahan | 2010a | West and Central | IFAT | 1:50 | 233 | 24 | 10.30 |
| Chaharmahal and Bakhtiar, Isfahan | 2011 | West and Central | ELISA | S/P ≥ 0.5 | 548 | 159 | 37.90 |
| Razavi Khorasan | 2009 | Northeast | PCR | Gene- 5Nc5 | 174 | 4 | 2.20 |
| Khuzestan | 2019 | Southwest | ELISA | S/P ≥ 0.5 | 100 | 18 | 18.00 |
| Chaharmahal and Bakhtiar, IFAT | 1:50 | 200 | 55 | 27.50 |
| Isfahan | 2017 | Center | ELISA | S/I ≥ 0.153 | 113 | 20 | 17.69 |
| Hamedan | 2014a | West | ELISA | S/P ≥ 0.5 | 360 | 36 | 10.00 |
| Hamedan | 2014 | West | IFAT | 1:50 | 270 | 73 | 27.00 |
| Chaharmahal and Bakhtiar, IFAT | 1:50 | 108 | 59 | 54.62 |
| Kerman | 2015 | Center | ELISA | S/P ≥ 0.5 | 185 | 16 | 8.60 |
| Tehran | 2017 | North | IFAT | 1:50 | 100 | 32 | 32.00 |
| East Azerbaijan | 2012 | West | IFAT | 1:50 | 100 | 31 | 31.00 |
| Lorestan | 2014 | West | PCR | Gene- 5Nc5 | 428 | 9 | 2.10 |
| Isfahan | 2017 | Center | PCR | Gene- 5Nc5 | 100 | 22 | 22.00 |

**Table 1:** Continued

**Notes:**
- **Year of the pub (year of publication):**
- **IFA (Indirect immunofluorescent Assay):**
- **ELISA (Enzyme-Linked Immunosorbent Assay):**
- **S/I (Sample Index values):**
- **PP (Percent Positivity):**
- **S/P (Sample to Positive ratios):**
- **AV (Absorbance Values):**
- **IgG (Immunoglobulin G):**
- **PCR (Polymerase Chain Reaction):**
**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 I² 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.
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)
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 I² = 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

![Forest plot diagram showing portion meta-analysis plot of N. caninum infection prevalence in dogs in Iran (random-effects)](image)
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

| Probable source of heterogeneity | Cattle Multivariate | Cattle Univariate | Dog Multivariate | Dog Univariate |
|---------------------------------|---------------------|-------------------|-----------------|---------------|
| Year                            | -0.0092731          | 0.076             | -0.0060815      | 0.225         |
| Sample size                     | -0.0000036          | 0.722             | 0.0004783       | 0.041         |
| Districts                        | -0.0166418          | 0.029             | -0.0133732      | 0.065         |
| Province                         | 0.0023875           | 0.539             | 0.0041939       | 0.233         |
| Detection method                 | -0.1722615          | 0.128             | -0.0865771      | 0.358         |
| Testing cut-off levels           | 0.0177409           | 0.395             | 0.0136295       | 0.434         |
| Type of array                    | -                 | -                 | -0.0000541      | 0.364         |

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

| Districts | Cattle Pooled prevalence | 5% Confidence interval | Dog 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                  | 10.5-51.2              |
| Southeast | 9.3                      | 4.3-14.3               | -                     | -                      |

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

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**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 version 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.

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