Seroprevalence of bovine herpesvirus type 1 among cattle population in Iran; A systematic review and meta-analysis

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Abstract

Bovine herpesvirus type 1 (BHV-1) is the causative agent of several clinical manifestations including Infectious Bovine Rhinotracheitis, infectious pustular vulvovaginitis/balanoposthitis, conjunctivitis, encephalitis, abortion, infertility, mastitis, enteritis, dermatitis and the systemic form of the infection in newborn calves. Although many investigations regarding prevalence of BHV-1 infection in cattle in Iran have been conducted, until now there is the lack of comprehensive information on the BHV-1 status in Iran. We aimed to present the seroprevalence on BHV-1 in cattle population in Iran based-on a systematic review and meta-analysis study and also to give profitable outputs in formulating the infection control strategies. The meta-analysis study was conducted in national and international databases to find articles which evaluated BHV-1 seroprevalence by antibody-captured ELISA in cattle in Iran by searching terms including Bovine herpesvirus type 1, cow, cattle, bovine, Iran, epidemiology and prevalence alone or in combination in both English and Farsi language. After reviewing of 124 published documents, a total of 25 studies from 20 documents were eligible to be included in this meta-analysis study. Analysis was done using the Comprehensive Meta-Analysis V.3 software. The total seroprevalence of BHV-1 in apparently healthy cattle at animal and herd level based on ELISA test was 40.2% (95% CI= 32.3–48.6) and 75.5% (95% CI= 63.9–84.2), respectively. A well-defined control strategy for

preventing and controlling BHV-1 infection in Iran should be based on further studies on BHV-1 epidemiology, control of animal and semen importation, using marker vaccine and planned biosecurity measures to control the epidemiological risk of infection due to the presence of BHV-1 latent carriers.

Keywords: BHV-1, Seroprevalence, Cattle, Meta-analysis, Iran

1. Introduction

Bovine herpesvirus type 1 (BHV-1) is an enveloped DNA virus, a member of genus Varicellovirus in the subfamily Alphaherpesvirinae, which belongs to the Herpesviridae family in the order Herpesvirales. Based on the genomic analysis and viral peptide patterns, four different serotypes of BHV-1 have been characterized of which respiratory subtype the subtype BHV-1.1 is associated with respiratory disease, subtypes BHV-1.2a and BHV-1.2b are related to genital disease and BHV-1.3 related to neurological disorders that has been reclassified as three genotypes, BHV-5a, BHV-5b, and BHV-5non-a/non-b (1–3).

The virus is the cause of multiple clinical signs in cattle populations worldwide, however; other *Artiodactyla* may be infected with BHV-1 and show clinical signs (4).

The disease associated with the BHV-1, is an OIE-listed B disease, may show several clinical manifestations including inflammatory reactions in both respiratory (Infectious Bovine Rhinotracheitis) and genital tracts (infectious pustular vulvovaginitis/balanoposthitis), conjunctivitis, encephalitis, abortion, infertility, mastitis, enteritis and dermatitis. Also, the systemic form of the infection affecting visceral organs may develop in newborn calves (5–7). When the disease occurs in unvaccinated dairy cattle, the incidence of the morbidity and case-fatality rates 8% and 3% respectively, but morbidity and mortality are higher in feedlot cattle (8).

The infection is mainly transmitted via the nasal exudate and coughed-up droplets, ocular and genital secretions, fresh or frozen semen as well as contaminated equipment and fetal fluids and tissues (9,10).

The BHV-1 virus is able to establish lifelong latency after a primitive infection with a field isolate or vaccination with an weakened strain and stressful conditions such as transportation,

parturition and glucocorticoid therapy may lead to reactivation and shedding of the virus complicating control and eradication strategies (11,12).

In Iran, BHV-1 for the first time reported in 1964-8 based the clinical observations and serology (13). In 1973-5 BHV-1was isolated from nasal secretions of imported cows with an acute respiratory disease (14). Since then, BHV-1 infection reported from several provinces and union territories of the country. As reports are available from different provinces in different time-periods, the unified data on the status of BHV-1 infection in Iran is missing. To address this critical knowledge gap, a systematic review and meta-analysis was conducted to determine the seroprevalence of BHV-1 infection in cattle population of Iran and also to give profitable outputs in formulating the infection control strategies.

2. Material and Method

2.1.Database search

For gathering information, articles regarding seroprevalence of bovine herpesvirus type 1 in apparently healthy cattle in Iran based on antibody-captured ELISA test in both English and Farsi language were searched in nine databases were included: four English databases (PubMed, Google Scholar, Science Direct, Web of Science and Scopus) and four Persian databases (Magiran, Irandoc and the Scientifc Information Database [SID]) for the articles published prior to November 2023. We also checked out dissertations and all abstract books of scientific conferences in Iran from 2000 to 2023. In order to avoid missing any articles, the citations of the included articles were reviewed to seek out other relevant studies. The searched terms were; “Bovine herpesvirus type 1”, “cow”, “cattle”, “bovine”, “Iran”, “epidemiology”, and “prevalence” alone or combined together with "OR" and/or "AND".

2.2.Data collection

Figure 1 shows the items used for the meta- analysis study (PRISMA) process (Fig. 1). After screening the titles and abstracts of articles identified by the initial search, those that describe the seroprevalence of BHV-1 by antibody-captured ELISA test in apparently healthy cattle (cattle of all ages, irrespective of their breed) in Iran were considered for the study. Studies with other purposes, such as those with other animal species as target populations, those evaluating the molecular characteristics of the isolated virus and studies for detection of the virus or antibody in milk, in semen or in aborted fetuses were excluded. In the next step, for quality assessment of eligible studies, the Strengthening the Reporting of Observational Studies

in Epidemiology (STROBE) checklist were used. For each study, the following data was extracted: first author's name, publication date, location of study, sample size, number of positive, study type, herd type, age of samples and BHV-1 vaccination. Then the studies were grouped based on animal level i.e. individual and herd (Table 1).

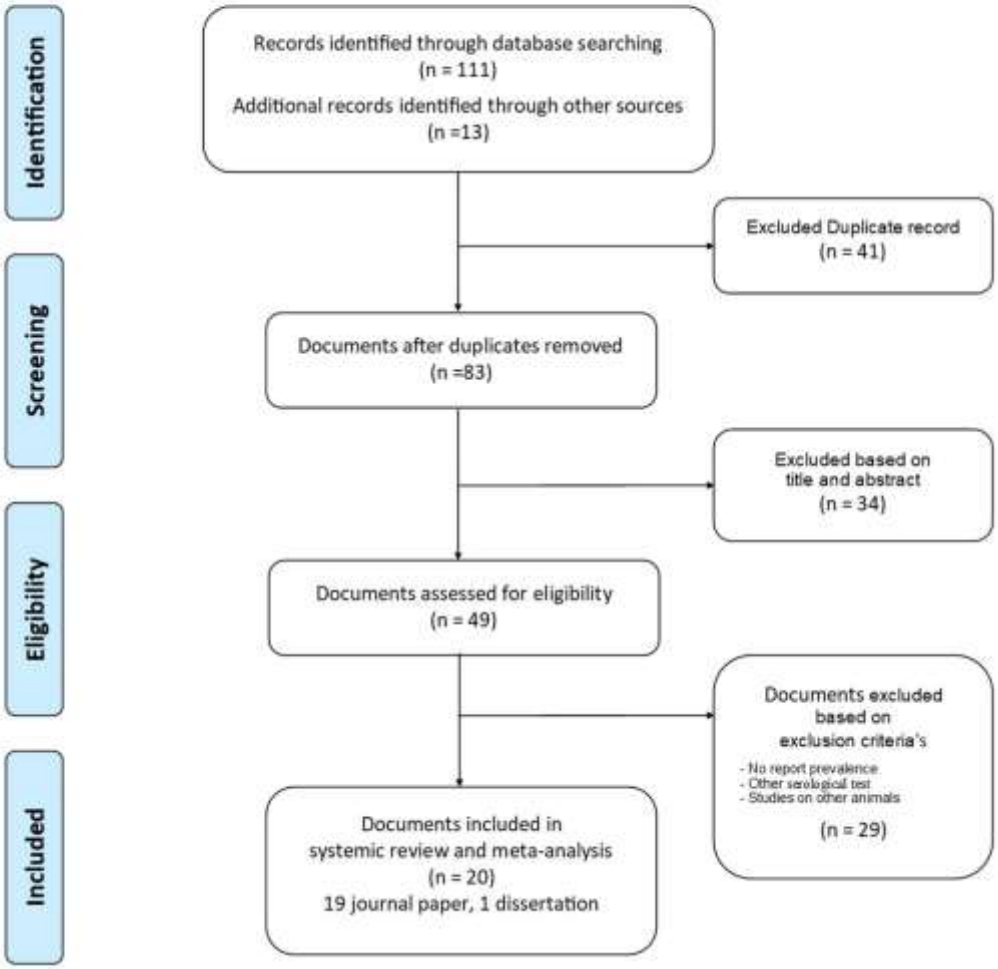

Figure 1. PRISMA flow diagram (included and excluded records)

106 Table 1. Documents included in the meta-analysis for serologic prevalence of BHV-1 in
107 cattle population in Iran

Study area	Herds (p/s)	Animals (p/s)	Herd type (sampling age (month)), BoHV-1 vaccination	Study design	Reference
West Azerbaijan	18/22	65/190	NA	Retrospective	(15)
Kurdistan	-	169/454	NA	Cross-sectional	(16)
Khuzestan	-	180/572	NA	Cross-sectional	(17)
Khorasan Razavi	-	89/150	Dairy (> 24)	Cross-sectional	(18)
Kerman	5/15	55/181	Dairy (12-36), No	Cross-sectional	(19)
Fars	39/39	237/856	Dairy (> 12), No	Cross-sectional	(20)
Isfahan	-	462/642	Dairy (> 0), No	Cross-sectional	(21)
Fars	-	20/56	NA	Cross-sectional	(22)
Khuzestan	-	28/50	NA	Cross-sectional	(22)
Kohgilooye va Boyer Ahmad	-	12/29	NA	Cross-sectional	(22)
Different regions [a]	13/15	314/558	Dairy, beef (12-48), No	Cross-sectional	(23)
Markazi	11/12	286/803	Dairy (> 12), No	Cross-sectional	(24)
Qazvin	5/8	36/504	Dairy (12-48), No	Cross-sectional	(25)
Hamedan	34/41	289/492	Dairy (> 6), No	Cross-sectional	(26)
Chaharmahal va Bakhtiari	-	103/192	Dairy	Cross-sectional	(27)
Khorasan	-	88/290	Dairy	Cross-sectional	(27)
Semnan	-	72/306	Dairy	Cross-sectional	(27)
Sistan and Baluchestan	-	35/94	Dairy	Cross-sectional	(27)
Fars	-	182/184	NA	Cross-sectional	(28)
Khuzestan	-	260/534	(> 0), No	Cross-sectional	(29)
Zanjan	8/10	64/562	(> 0), No	Cross-sectional	(30)
Isfahan	16/16	156/216	Dairy (> 12), No	Cross-sectional	(31)
Fars	13/18	167/420	Dairy (> 0), No	Cross-sectional	(32)
Qazvin	9/16	52/1017	Dairy (> 12), No	Cross-sectional	(33)
Yazd, South Khorasan	50/76	400/800	Dairy (> 12), No	Cross-sectional	(34)

108 NA: Not available

109 p/s: No. of positive/sample

110 a: Yazd, Khorasan, Fars, Markazi, East Azerbaijan and Qom

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2.3.Statistical analysis

We estimated the pooled seroprevalence of Bovine herpesvirus type 1 in cattle by either the fixed-eff ects or random-eff ects model with 95% confidence interval and a significant level of 5%, and they are displayed using the FORST PLOT accumulation chart. Heterogeneity of included studies was performed using the Cochran's heterogeneity statistic (Q-test) and I^2 statistic. Egger's regression test was used to assess possible publication bias. Analysis was done using the Comprehensive Meta-Analysis V.3 software.

3. Results

As presented in Fig. 1, initially, a total of 124 documents were collected. In secondary screening, based on title and abstract, 41 duplications were removed and 83 remained for full-text review. Of those, 34 documents based on title and abstract and 29 documents based on the selection criteria were excluded. Finally, a complete of 25 studies from 20 documents were eligible to be included in this meta-analysis study (Table 1). Based on us analyze, evidence of publication bias was not observed (P = 0.295) (Figure 2).

The provinces where seroprevalence of BHV-1 among cattle in Iran was studied, was showed in Fig 3. The total seroprevalence of BHV-1 in apparently healthy cattle at animal level based on antibody-captured ELISA test, was reported in 25 studies. Our analysis included a total of 10,151 cattle and the overall prevalence of BHV-1, based on the random-effects model (I^2 = 98.20, Q test P = 0.00), was 40.2% (95% CI= 32.3–48.6) (Figure 4). Also, the total prevalence of BHV-1 infection at herd level, was reported in 12 studies and 288 herds and the overall prevalence based on the random-effects model (I^2 = 61.56, Q test P = 0.00), was 75.5% (95% CI= 63.9–84.2) (Figure 5).

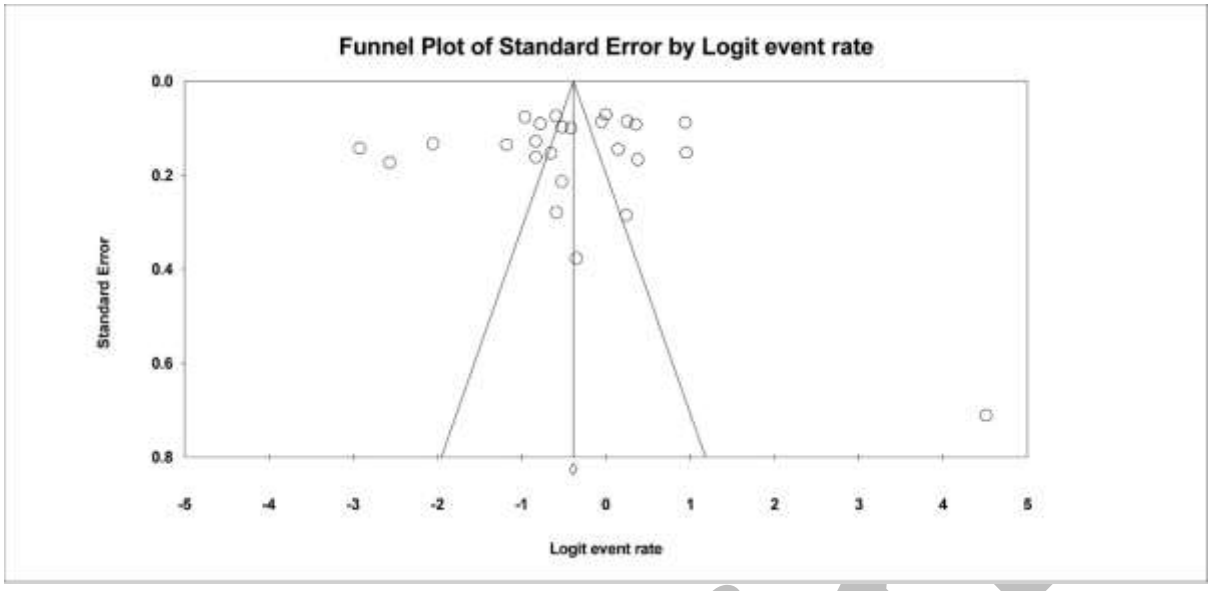

Figure 2. Funnel Plot to Assess Publication Bias

Figure 3. The provinces where seroprevalence of BHV-1 among cattle in Iran was studied

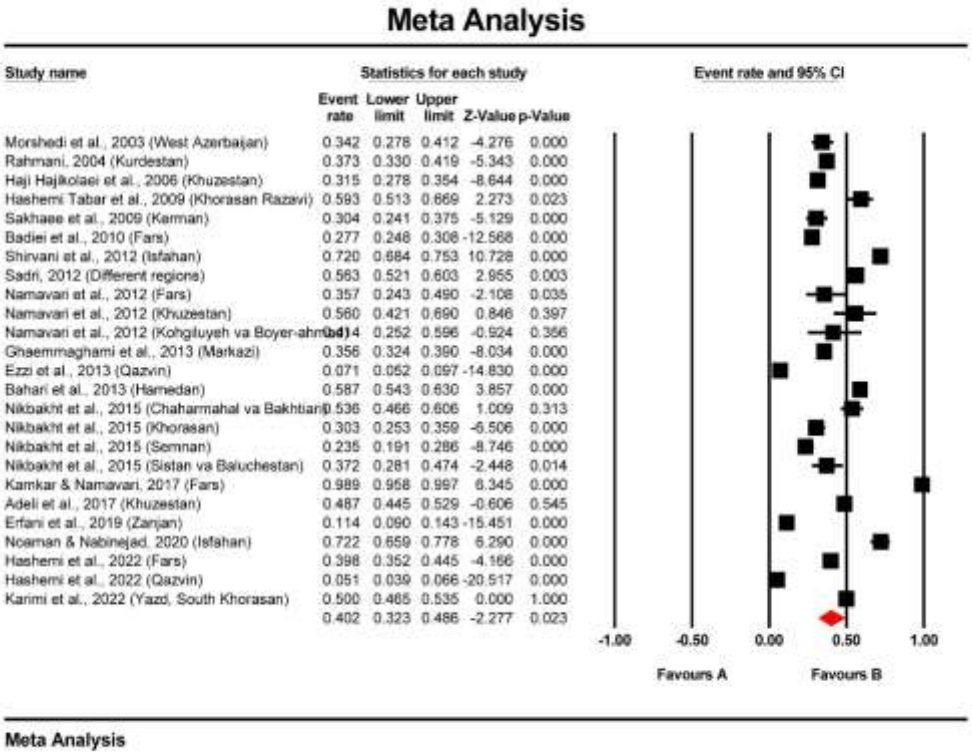

Figure 4. Forest plot for the seroprevalence of BoHV-1 in cattle population at animal level in Iran

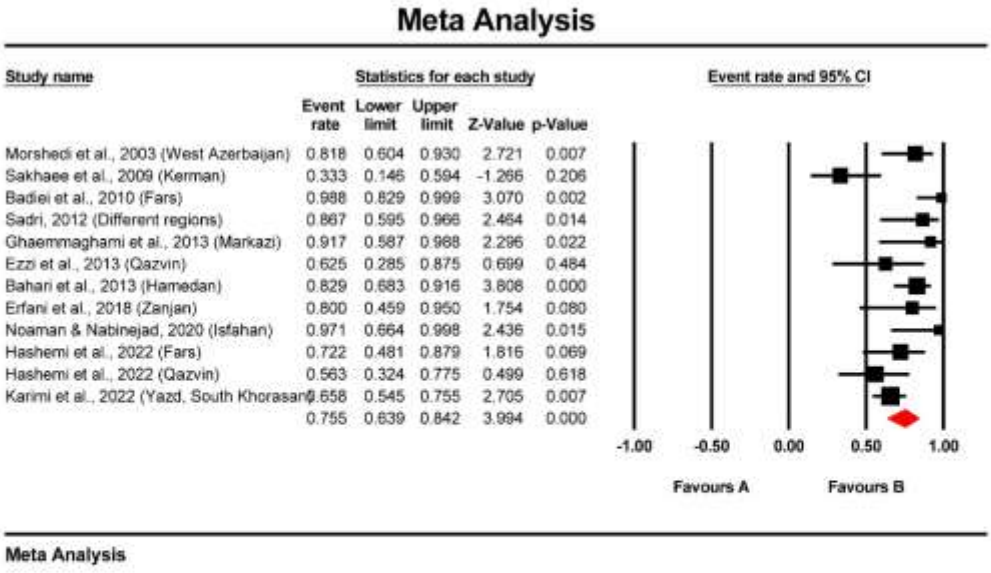

Figure 5. Forest plot for the seroprevalence of BoHV-1 in cattle population at herd level in Iran

4. Discussion

According to the report of Iranian Ministry of Agriculture (2018), there are approximately 8,000,000 cattle of three groups of cattle breeds in Iran, including pure exotic, crossbred of native and exotics and pure native breeds that kept in industrial, semi-industrial and traditional husbandry systems. The most important breed bred is the Holstein, with an estimated annual milk and meat production of approximately 1,059,000 and 830 (×1000 tons), respectively.

From 1964-70 to date, BHV-1 antibody detected in cattle, sheep, goat, buffalo, camel, pig and horse and isolated from cattle in Iran (13,35). So far, a number of research has been carried out on cattle in various parts of Iran (Table 1), to our knowledge, this is the first meta-analysis of the global prevalence of BHV-1 infection in apparently healthy cattle based on ELISA test in Iran.

There are differences between the reports of the seroprevalence rate from various countries and areas. Probably, this result might be associated with weather condition, geographical situation,

sample size, sampling season, diagnostic methods, diversity of breed, age and sex and husbandry systems. It is reported that colder and higher altitude area can acts as a risk factor for cattle herds to have experienced BHV-1 infections (36). It is well known that all breeds of cattle at any age are susceptible to BHV-1 infections, however; the disease is prevalent in older animals, probably because of their greater exposure to natural sources of infection and loss of maternal immunity (8).

In light of our outcomes, the seroprevalence of BHV-1 among cows and herds was 40.2% (95% CI= 32.3–48.6) and 75.5% (95% CI= 63.9–84.2) respectively in Iran. The pooled prevalence of BHV-1 was higher than the previous study has been carried out on 9968 sera collected from the whole country using serum neutralization test that the rate of infection was estimated as 30.6% (37), which shows that the situation of BHV-1 infection in Iran has become more and more serious in recent years.

There are many serologic reports in cattle population from around the world. Based on a review on epidemiology and control of BHV-1 infection in Europe (6), the serologic prevalence has been reported in cows from as low as 12% in Scotland to very high rate (77.5%) in Southern Italian Apennines and in herds from as low as 22% in Estonia to very high rate (100%) in Central Italy. The pooled estimate of seroprevalence of BHV-1 at animal and herd level in Iran in comparison with the other countries, shows that Iran could be considered among the intermediately infected countries.

BHV-1 infection can cause major economic consequences in cattle breeding herds including abortion, infertility, loss of production and deaths. The costs of treatment, preventive and control measures should also be taken into account (38).The most prevalent reason of culling cows in Iran is frequent abortion and reproductive failure (39). Occurrence of high prevalent abortion in cattle population of Iran (11.1-18.6%) has multifactorial etiologies (40). However, some researchers (41–44) believe that BoHV-1 can act as an abortion pathogen in cattle, as BoHV-1 DNA was isolated between 6.8 to 100% of aborted fetuses in different regions of Iran.

The control and eventual eradication of BoHV-1 is based on the detection and removal of infected animals, with or without the use of marker vaccines but this is inefficient for eradication of infection in countries with large herds or high seroprevalence of BHV-1. Alternatively, repeated vaccination of infected herds can be undertaken to increase protection, reduce the effects of disease, and reduce the risk of re-excretion by latently infected animals (26,45).

In conclusion, the endemicity of BHV-1 infection in cattle population of Iran with the high prevalence in herds and animals found in this study suggested necessity of an intensive control program for reducing BHV-1 infection rates. Based on present findings, there are no national IBR/IPV control programs in Iran. A well-defined control strategy for preventing and controlling BHV-1 infection in Iran should be based on further studies on BHV-1 epidemiology, control of animal and semen importation, using marker vaccine and planned biosecurity measures to control the epidemiological risk of infection due to the presence of BHV-1 latent carriers.

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Ethics

We hereby declare all ethical standards have been respected in preparation of the submitted article.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Data Availability

The data that support the findings of this study are available on request from the corresponding author.

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