Research Article

Serological Evidence of Bluetongue in Iran: A Meta-Analysis Study

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Abstract | Bluetongue is an infectious viral disease that is endemic in the domestic livestock populations of all tropical and subtropical countries. BT was first reported in Iran in 1972, however until now there is the absence of comprehensive information on the BT status in Iran. We aimed to present the seroprevalence on BT in farm animals of Iran based-on a meta-analysis study. The meta-analysis study was conducted in national and international databases to find articles which evaluated bluetongue seroprevalence by antibody-captured ELISA test in livestock in Iran by searching terms including bluetongue, sheep, ovine, goat, caprine, cow, cattle, bovine, buffalo, camel, Iran and prevalence alone or in combination in both English and Farsi language. After reviewing 82 published articles, a total of 48 studies from 29 articles were eligible to be included in this meta-analysis study. The total seroprevalence of bluetongue in apparently healthy sheep, goat, cow and camel at animal level based on ELISA test was 50.4% (95% CI= 43.5–57.2), 79.2% (95% CI= 70.7–85.8), 3.3% (95% CI= 0.6–15.0) and 44.8% (95% CI= 20.8–71.5), respectively. The estimated pooled odds ratios between abortion history and bluetongue infection estimated among sheep (OR=1.75, 95 % CI= 0.84 to 3.68) and goat (OR=2.93, 95 % CI= 1.26 to 6.80). A well-defined control strategy for preventing and controlling BTV spread in Iran should be based on further studies on BT epidemiology and BTV serotypes, vector control, animal movement restrictions and vaccination program to reduce.

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Introduction

Bluetongue (BT) is a noncontagious, insect-borne disease caused by an Orbivirus of the family Reoviridae. Its transmitted by midges of a couple of select *Culicoides* species and its worldwide dispersion is to a great extent characterized by appropriate climatological factors for these species (Purse *et al.*, 2005; Sperlova and Zendulkova, 2011). Bluetongue virus (BTV) infection involves domestic and wild ruminants such as sheep, goats, cattle, buffaloes, deer, most species of African antelope and various other Artiodactyla such as camels (Constable *et al.*, 2017; Mellor *et al.*, 2008). Already 27 different serotypes of bluetongue virus (BTV) have been characterized of which 24 typical serotypes and other atypical novel BTV serotypes including BTV-25 (Toggenburg virus strain), BTV-26, BTV-27 (variants 01, 02 and 03), BTV-29, BTV-XJ1407, and BTV-X ITL2015 have been described and reported throughout the world (Schulz *et al.*, 2008; Rupner *et al.*, 2020). BT is a notifiable disease of the World Organization for Animal Health (OIE) as "A" list of diseases, because of considerable morbidity and mortality rates

in infected animals and the potential to cross the geographical boundaries of countries (OIE, 2008). When the disease occurs in a flock for the first time, the incidence of clinical disease may reach 50% to 75% and the mortality 20% to 50% but in enzootic areas, the disease is much less severe and often unapparent (Constable *et al*., 2017).

Sheep infected with bluetongue virus may remain asymptomatic, or grow to be mildly to severely ill. The clinical signs and symptoms vary depending on viral strain and sheep breed and only a little percentage of viraemic sheep may develop clinical signs. Common clinical signs encompass depression, anorexia, fever (as much as 42 ˚C), tachypnea, excessive salivation, hyperaemia of the lips and nostrils, conjunctiva and serous nasal discharge which dries and forms crusts round the nose. Oedema of the tongue, lips, submandibulum and once in a while ears appear and lenticular necrotic ulcers develop, mainly on the lateral aspects of the tongue. The tongue is every so often cyanotic in intense cases, and may protrude from the mouth. Foot lesions, including laminitis and coronitis and manifested by lameness and recumbency, appear only in some animals, typically whilst when the mouth lesions begin to heal. Torticollis, dermatitis and breaks in the wool may also develop. Contamination in the pregnant ewes may prompt abortion, foetal mummification and the birth of weak lambs with CNS lesions, retinal lesions and/or skeletal malformations (Constable *et al*., 2017; Ganter, 2014; Oryan *et al*., 2013; Sperlova and Zendulkova, 2011).

Infections in cattle and goats are commonly subclinical in endemic areas, despite the fact that a few BTV strains, which include serotype 8, are highly virulent in cattle. Clinical cases in cattle and goats resemble the disease in sheep, however tend to be milder (Constable *et al*., 2017). Reports of BTV seropositive camels have been detailed from a wide range of countries but limited clinical symptoms or pathological lesions resulting from BTV had been described (Wernery and Kaaden, 2002). These animals are important in the epidemiology of the disease due to the prolonged viraemia in the absence of clinical ailment (Oryan *et al*., 2013).

The first proof of BT in sheep was recorded by Hesami and Ghabousi, 1972 (unpublished material). They reported that the disease had been suspected in sheep and goat by some government veterinarians in parts of Iran based totally on the clinical discoveries (Hassani and Hamedi, 2019, 2020). The primary serological study led by Afshar and Kayvanfar (1974) in Tehran and Fars utilizing Immuno-gel diffusion test, in which 7.6%, 13.6%, 0.6%, 5.9%, 4.5% and 0% in sheep, goat, cattle, camel, pig and buffalo was positive for BTV antibodies respectively (Afshar and Kayvanfar, 1974). Some studies have been administered on the presence of BTV antibodies in sheep and goats in various areas of Iran that mostly mentioned high incidence of BT and to date, serotypes 3, 4, 7, 9, 16, 20 and 22 of BTV have been reported in Iran (Azimi *et al*., 2008, 2011; Khezri and Azimi, 2012; Moakhar *et al*., 1988).

The prevalence of an infection at the herd or animal level is a key issue determining whether or not the infection ought to be considered crucial and which measures and policies must be made and applied. In view of the reports on BT are available from different areas and time-periods, comprehensive information on the BT status in Iran is absent. To eliminate this critical knowledge gap, a meta-analysis study was performed to determine the BT seroprevalence in farm animals of Iran and, to give significant contributions to figuring the disease control strategies.

Materials and Methods

Introduction to the study area Iran

The country is located in the Middle East, western Asia between latitudes 24–40 N, and longitudes 44–64 E with an area of 1,648,195 km^2 and shares borders with Armenia, the Azeri exclave of Nakhichevan, and the Republic of Azerbaijan, Turkmenistan, Afghanistan, Pakistan, Iraq and Turkey. Iran's climate is diverse, ranging from arid and semi-arid in central, eastern and southern regions, to subtropical in the north on the coast of the Caspian Sea which is covered by the lush lowland and the vast forests and more than +50˚C in summer to -40˚C in winter in some areas. There are two large deserts in the central region with nearly no rain, and vice versa more than 2000 mm raining per year on the northern edge of the country (the Caspian coastal plain).

Search strategy

This study become performed using a meta-analysis survey in which articles regarding seroprevalence of bluetongue in apparently healthy livestock (sheep, goat, cow, buffalo and camel) of Iran based on antibody-captured ELISA test in both English and

Farsi language were searched in data banks of Google Scholar (scholar.google.com), PubMed (www.pubmed.gov), Science Direct (www.sciencedirect.com), Scopus (www.scopus.com), Web of science (ipscience.thomsonreuters.com/product/web-of-science), Scientific Information Database (www.sid.ir), Magiran (www.Magiran.com) and Iranian Research Institute for Information Science and Technology (www.irandoc.ac.ir) for the articles published prior to 25 April 2020. Additionally, the citations of the included articles from these databases were reviewed to seek out other relevant studies. We also checked out the electronic abstract list of congresses conducted in Iran and also the electronic database of students' thesis and unpublished researches with an email to researchers. The searched terms were; bluetongue, sheep, ovine, goat, caprine, cow, cattle, bovine, buffalo, camel, Iran, and prevalence alone or combined with OR and/or AND.

Study selection and data extraction

The titles and abstracts of articles identified by the initial search were screened and those that did not describe the seroprevalence of bluetongue by antibody-captured ELISA test in apparently healthy sheep, goat, cow, buffalo and camel in Iran were removed. Figure 1 shows the items used for the meta-analysis study (PRISMA) process (Figure 1). In the next step, the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist were used for the assessment of the quality of reporting. For every study, the following information was extracted separately: Name of the first author, publication date, place of study, sample size and number of positive. Then the studies were grouped based on host animal, namely sheep, goat, cow, buffalo and camel (Tables 1 and 2).

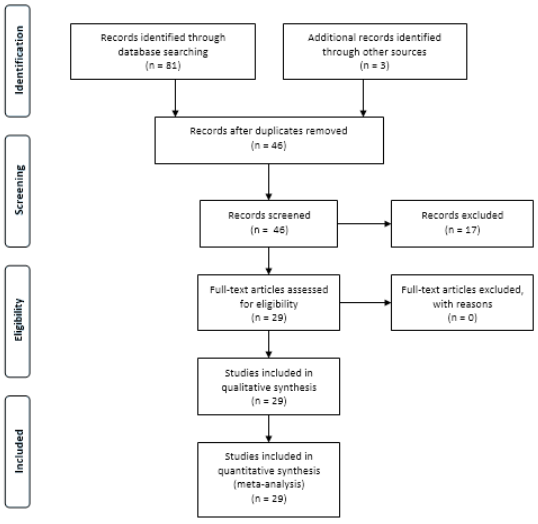

Figure 1: *PRISMA flow diagram (included and excluded records).*

Statistical analysis

The analysis was done using the Comprehensive Meta-Analysis V.2 software. The value of the index in each study and the estimated overall estimate (prevalence) were obtained with a random model or fixed model with a 95% confidence interval and a significant level of 0.05, and they are displayed using the FORST PLOT accumulation chart. The Cochran's heterogeneity statistic (Q-test) and I^2 statistics were used to examine the heterogeneity of studies. Publication bias was evaluated by Egger's regression test. To look at the connection between prevalence of BT infection and publication year, meta-regression model was used. Also, by calculating the global prevalence of bluetongue in each province, we mapped prevalence of bluetongue in each animal group.

Results and Discussion

Search results

Initially, a total of 84 articles were collected. In secondary screening, after putting off duplications (n = 38) based on title and abstract, 46 remained for full-text review. Of those, 17 articles were excluded based on the selection criteria, mainly relying on serological test (n = 10). Finally, a complete of 48 studies from 29 articles were eligible to be included in this meta-analysis study.

Seroprevalence of bluetongue in sheep

The total prevalence of bluetongue in apparently healthy sheep at an animal level based on antibody-captured ELISA test, was reported in 31 studies from 16 provinces of Iran. There was no significant publication bias (p = 0.165) and high heterogeneity (I^2 = 97.99, Q test p = 0.00) were observed. Our analysis included a total of 12,710 sheep and the overall prevalence of bluetongue, based on the random-effects model, was 50.4% (95% CI= 43.5–57.2) (Table 3, Figure 2). The highest and lowest seropositivity was seen in Khorasan Razavi province (89.7%, 95% CI: 87.2–91.7) and Qom province (12.1%, 95% CI: 7.7–18.4), respectively (Figure 3). Based on meta-regression analysis, the relationship between year of publication with the prevalence of BTV in sheep population in Iran is statistically significant, so the prevalence of BTV in Iran on a mild slope is increasing. (Slope= 0.04, p=0.00). Of 31 studies, only 8 studies in sheep investigated bluetongue infection by abortion history and statistical analysis revealed that there wasn't a

Table 1: *Characteristics of the included studies in the systematic review at animal level.*

Animal type	Study area	Climate	No. of positive/sample	Reference
Sheep	East Azerbaijan	Cold	636/832	Hassanpour *et al.*, 2008
	Isfahan	Hot and dry	269/504	Noaman *et al.*, 2008
	West Azerbaijan	Cold	400/1153	Jafari-Shoorijeh *et al.*, 2010
	Charmahal-va-bakhtiari, Khuzestan, Isfahan	Cold, hot and humid, hot and dry	265/770	Momtaz *et al.*, 2011
	Kurdistan	Cold	58/300	Khanbabaie *et al.*, 2011
	West Azerbaijan	Cold	548/981	Sadri, 2012
	Kurdistan	Cold	70/135	Khezri and Azimi, 2012
	Ilam	Cold	104/237	
	Kurdistan	Cold	123/268	Khezri, 2012
	Fars	Hot and dry	78/107	Mohammadi *et al.*, 2012
	Ardabil	Cold	29/122	Khezri and Azimi, 2013
	East Azerbaijan	Cold	79/198	
	West Azerbaijan	Cold	48/74	
	Kurdistan	Cold	63/151	
	Ilam	Cold	90/211	
	Khuzestan	Hot and humid	3/20	
	Qom	Hot and dry	18/149	
	Fars	Hot and dry	18/71	
	Khorasan Razavi	Cold	603/672	Najarnezhade *et al.*, 2013
	Fars	Hot and dry	610/820	Oryan *et al.*, 2013
	Kurdistan	Cold	126/297	Khezri *et al.*, 2014
	West Azerbaijan	Cold	71/198	Hasanpour *et al.*, 2014
	East Azerbaijan	Cold	134/200	Imandar *et al.*, 2014
	Khuzestan	Hot and humid	311/556	Noroozikia *et al.*, 2014
	Kohgiluyeh-va-Boyer-Ahmad	Cold	203/262	Sabaghan *et al.*, 2014
	Kerman	Hot and dry	32/37	Ezatkhah *et al.*, 2014
	Hormozgan	Hot and humid	8/12	
	Sistan va Bluchestan	Hot and dry	36/107	
	Charmahal-va-bakhtiari	Cold	462/928	Noaman and Arzani, 2017
	Fars	Hot and dry	1264/1782	Manavian *et al.*, 2017
	Hamedan	Cold	256/556	Yavari *et al.*, 2018
Goat	Isfahan	Hot and dry	182/370	Noaman *et al.*, 2008
	Fars	Hot and dry	69/93	Mohammadi *et al.*, 2012
	Khorasan Razavi	Cold	319/364	Najarnezhade *et al.*, 2013
	Fars	Hot and dry	162/190	Oryan *et al.*, 2013
	Kerman	Hot and dry	270/273	Ezatkhah *et al.*, 2014
	Hormozgan	Hot and humid	193/208	
	Sistan va Bluchestan	Hot and dry	182/215	
	Kerman	Hot and dry	63/93	Mozaffari *et al.*, 2014
	Charmahal-va-bakhtiari	Cold	776/1350	Noaman and Arzani, 2017
	Fras	Hot and dry	874/1569	Manavian *et al.*, 2017
Cattle	Kerman	Hot and dry	4/188	Mozaffari *et al.*, 2012
	Isfahan	Hot and dry	24/892	Noaman *et al.*, 2013
	Fars	Hot and dry	103/521	Manavian *et al.*, 2017
	Semnan	Hot and dry	0/184	Mohajer *et al.*, 2019
Camel (*Camelus dromedarius*)	Khorasan Razavi	Cold	10/56	Zibaei and Teimoori, 2012
	Yazd	Hot and dry	40/59	Mozaffari *et al.*, 2013
	Bushehr	Hot and humid	48/92	Manavian *et al.*, 2016

Table 2: *Characteristics of the included studies in the systematic review with and without abortion history.*

Animal type	Study area	Climate	No. of positive/ sample in with abortion history	No. of positive/ sample in non abortion history	Reference
Sheep	Fars	Hot and Dry	15/25	60/77	Mohammadi *et al.*, 2012
	Khorasan-Razavi	Cold	392/422	211/248	Najarnezhade *et al.*, 2013
	West Azerbaijan	Cold	38/80	26/92	Hasanpour *et al.*, 2014
	East Azerbaijan	Cold	49/66	62/94	Imandar *et al.*, 2014
	Khuzestan	Hot and Humid	11/23	268/481	Noroozikia *et al.*, 2014
	Kohgiluyeh and Boyer-Ahmad	Cold	56/65	116/136	Sabaghan *et al.*, 2014
	Chaharmahal-va-Bakhtiari	Cold	41/64	421/864	Noaman and Arzani, 2017
	Hamedan	Cold	232/360	24/196	Yavari *et al.*, 2018
Goat	Fars	Hot and Dry	33/42	34/49	Mohammadi *et al.*, 2012
	Khorasan-Razavi	Cold	202/222	117/142	Najarnezhade *et al.*, 2013
	Chaharmahal-va-Bakhtiari	Cold	74/83	702/1267	Noaman and Arzani, 2017

Table 3: *Seroprevalence of BT infection in farm animals in Iran.*

Animal type	No. of included studies	No. of tested animal samples	I^2	P-value for Heterogeneity	Global estimate (%) (95% CI)
Sheep	31	12710	97.99	0.00	50.4 (43.5-57.2)
Goat	10	4725	97.36	0.00	79.2 (70.7-85.8)
Cattle	4	1785	97.25	0.00	3.3 (0.6-15.00)
Camel (*Camelus dromedarius*)	3	207	92.43	0.00	44.8 (20.8-71.5)

Table 4: *The odds ratio of BT infection in animals with history of abortion in comparison with non-abortion history animals in Iran.*

Animal type	No. of included studies	No. of tested animal samples	I^2	P-value for Heterogeneity	Global estimate (%) (95% CI)
Sheep	8	5315	90.55	0.00	1.75 (0.84-3.68)
Goat	3	2967	73.48	0.02	2.93 (1.26-6.80)

significant association between abortion history and bluetongue infection among sheep (odds ratio (OR)= 1.75, 95 % CI= 0.84 to 3.68) (Table 4).

Seroprevalence of bluetongue in goat

The total prevalence of bluetongue in apparently healthy goats at an animal level based on antibody-captured ELISA test, was reported in 10 studies from 7 provinces of Iran. Significant publication bias (p = 0.00) and high heterogeneity (I^2 = 97.36, Q test p = 0.00) were observed. Our analysis included a total of 4,725 goats and the overall prevalence of bluetongue, based on the random-effects model, was 79.2% (95% CI= 70.7–85.8) (Table 3, Figure 4). The highest and lowest of seropositivity was seen in Hormozgan province (92.8%, 95% CI: 88.4–95.6) and Isfahan province (49.2%, 95% CI: 44.1–54.3), respectively (Figure 5). Meta-regression analysis revealed the statistically significant relationship between year of publication with the prevalence of BTV in goat population in Iran, so the prevalence of BTV in Iran on a mild slope is decreasing (Slope= -0.03, p=0.00). Of 12 studies, only 3 studies in goat investigated bluetongue infection by abortion history and statistical analysis revealed that there was a significant association between abortion history and bluetongue infection among goat (odds ratio (OR)= 2.93, 95 % CI= 1.26 to 6.80) (Table 4).

Seroprevalence of bluetongue in cattle

The total prevalence of bluetongue in apparently healthy cattle at an animal level based on antibody-captured ELISA test, was reported in 4 studies from 4 provinces of Iran. There was no significant publication bias (p = 0.144) and high heterogeneity (I^2 = 97.25, Q test p = 0.00) were observed. Our analysis included

a total of 1,785 cows and the overall prevalence of bluetongue, based on the random-effects model, was 3.3% (95% CI= 0.6–15.0) (Table 3, Figure 6). The highest and lowest of seropositivity was seen in Fars province (19.8%, 95% CI: 16.6–23.4) and Semnan province (0.0%, 95% CI: 0.0–4.2), respectively (Figure 7). Meta-regression analysis showed that the prevalence rate has a growing trend in cattle population in Iran (Slope= 0.51, p=0.00).

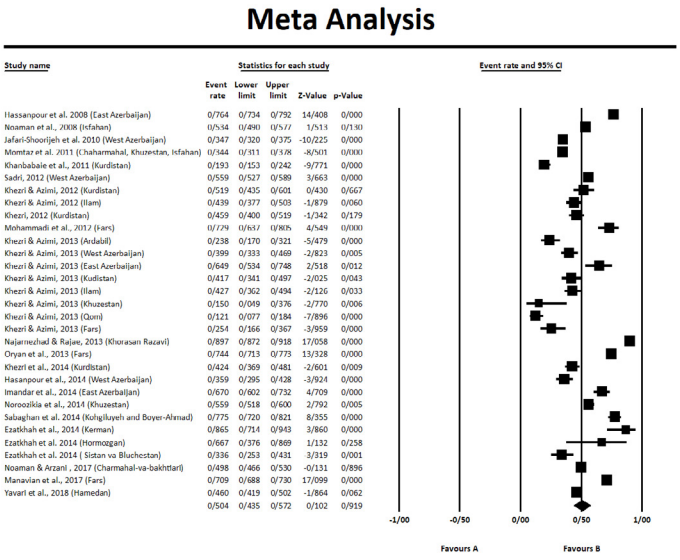

Figure 2: *Forest plot for the seroprevalence of bluetongue in sheep population at animal level in Iran.*

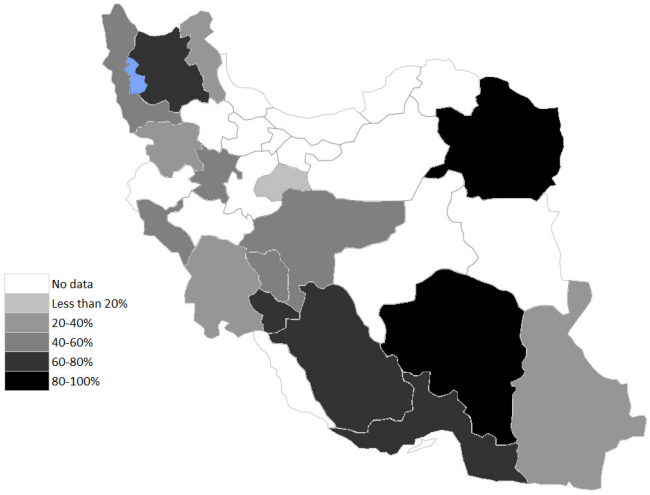

Figure 3: *Spatial distribution of bluetongue seroprevalence in sheep population at animal level in Iran.*

Seroprevalence of bluetongue in camel

The total prevalence of bluetongue in apparently healthy camels at an animal level based on antibody-captured ELISA test, was reported in 3 studies from 3 provinces of Iran. There was no significant publication bias (p= 0.30) and high heterogeneity (I^2= 92.43, Q test p= 0.00) were observed. Our analysis included a total of 207 dromedary camels and the overall prevalence of bluetongue, based on the random-effects model, was 44.8% (95% CI= 20.8–71.5) (Table 3, Figure 8). The highest and lowest of seropositivity was seen in Yazd province (67.8%, 95% CI: 54.9-78.4) and Khorasan Razavi provinces (17.9%, 95% CI: 9.9–30.1), respectively (Figure 9). Based on Meta-regression analysis, the relationship between year of publication with the prevalence of BTV in camel population in Iran has an increasing trend (Slope= 0.15, p=0.08).

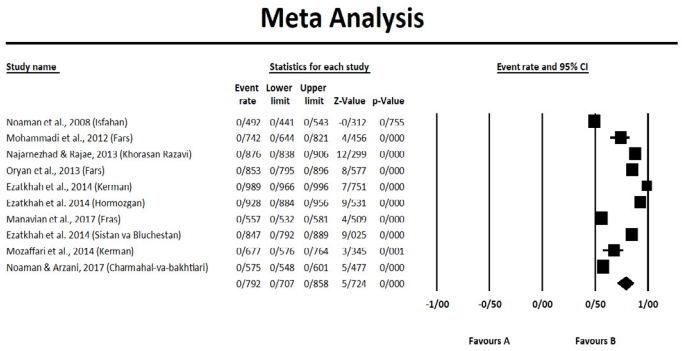

Figure 4: *Forest plot for the seroprevalence of bluetongue in goat population at animal level in Iran.*

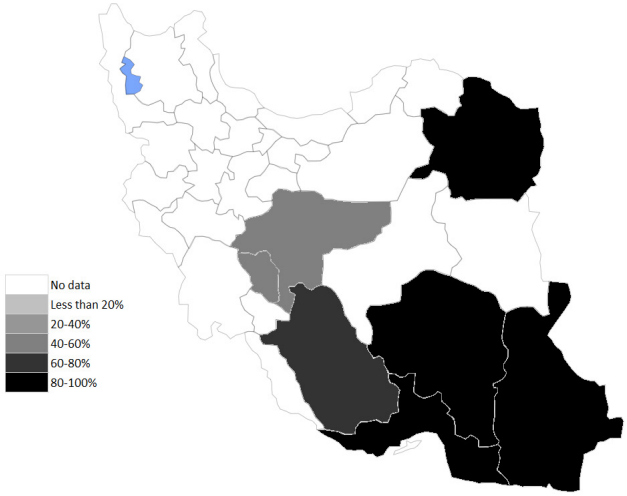

Figure 5: *Spatial distribution of bluetongue seroprevalence in goat population at animal level in Iran.*

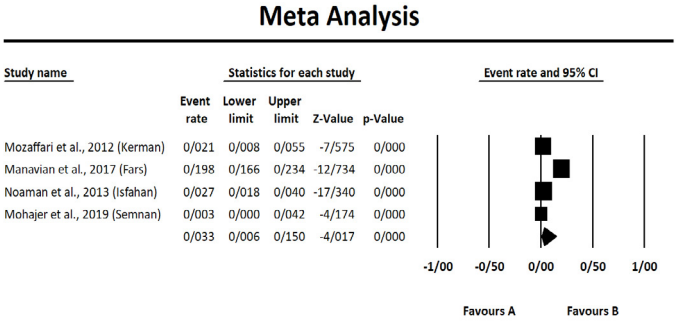

Figure 6: *Forest plot for the seroprevalence of bluetongue in cattle population at animal level in Iran.*

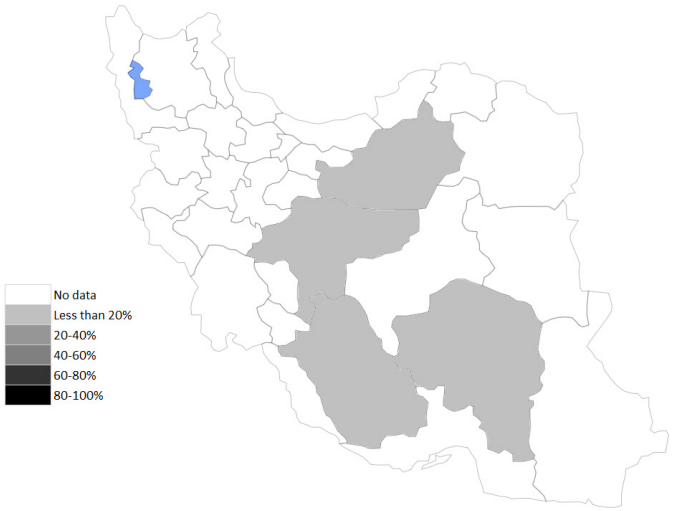

Figure 7: *Spatial distribution of bluetongue seroprevalence in cattle population at animal level in Iran.*

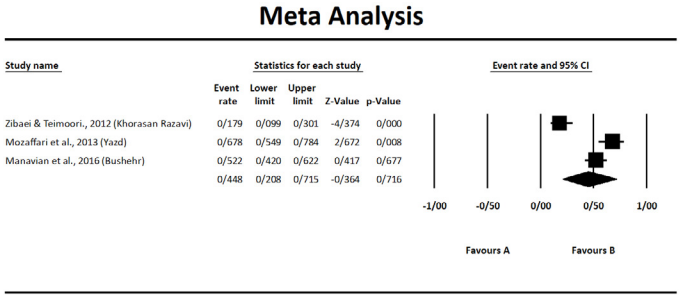

Figure 8: *Forest plot for the seroprevalence of bluetongue in camel population at animal level in Iran.*

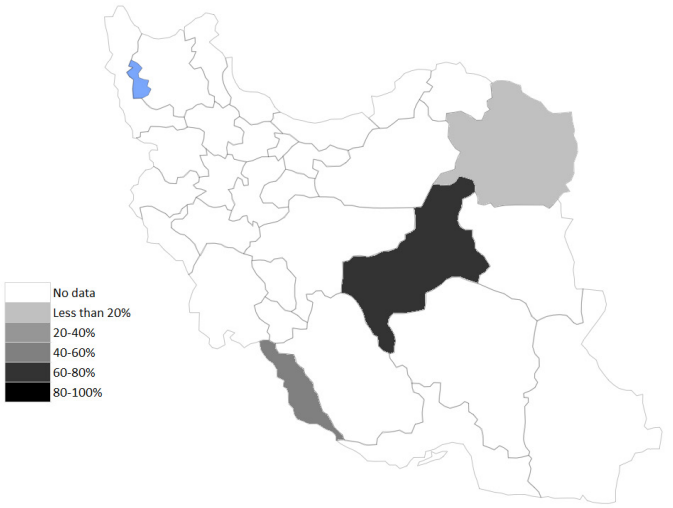

Figure 9: *Spatial distribution of bluetongue seroprevalence in camel population at animal level in Iran.*

In Iran, bluetongue was reported 1972-74 based on clinical findings serological survey in livestock, so far BTV detected in sheep, goat, cow, camel, pig and Mouflon (*Ovis orientalis*) and isolated from sheep (Hassani and Madadgar, 2020; Khezri and Bakhshesh, 2014). Since then many studies have been carried out on farm animals in various parts of Iran. This is the first comprehensive and meta-analysis study of the prevalence of bluetongue in apparently healthy domestic animals based on ELISA test in Iran. The sort of farmed animals included in the present study was sheep, goats, cow, buffalo and camel but we didn't any report concerning prevalence of bluetongue in buffalo.

In light of our outcomes, the seroprevalence of bluetongue among sheep and goat was 50.04% (95% CI= 43.5–57.2) and 79.9% (95% CI= 72.0–86.0) respectively in Iran. Unexpectedly, more goats than sheep resulted infected. Probably, this result might be associated with the weather condition, geographical situation, and altitude of the land and sampling season as these factors can change the activity of the *Culicoides* vectors and windborne carriage of infected *Culicoides* from distant endemic areas, diversity of species, breed, age and sex, ruminant husbandry systems and default manage on imported animals from neighborhood countries.

Serological evidence and the knowledge available on BT epidemiology and the distribution of the historical vector, *Culicoides imicola*, may indicate that BT is enzootic throughout the Middle East. The bluetongue disease has been recorded in some Middle-Eastern countries (Iran, Iraq, Saudi Arabia, Syria, Afghanistan, Oman, Pakistan, Turkey, Yemen, and Jordan). Within the Middle East, while BTV4 seems to be the predominant serotype involved in clinical disease, other serotypes have been identified in infected animals: 1, 2, 3, 6, 7, 8, 9, 10, 12, 16, 20, 22 and 24 (Al-Busaidy and Mellor, 1991; Ertürk *et al.*, 2004; El-Hage *et al.*, 2013; Hassani and Madadgar, 2020; Maan *et al.*, 2011; OIE, 2009). Numerous investigations have been performed in different parts of Turkey for BTV. The disease was detected serologically and virologically in many studies thus far and type 4, 9 and 16 were identified in Turkey. Besides, *C. imicola* continues to be the foremost prevalent vector in Turkey (Ertürk *et al.*, 2004). In Pakistan, the BTV seroprevalence was reported in sheep (47.3%) and goat (50.9%) and Serotype 8 was the most prevalent followed by an equal prevalence of serotypes 2 and 9 (Sohail *et al.*, 2018). Up to date, seroprevalence rates of BTV in sheep (68.6%) and goats (71.8%) from Afghanistan and 22.3-60-1% and 21.4-100 % of sheep and goat in Iraq was reported (Ali *et al.*, 2014; Shlash *et al.*, 2012).

The geographic situation of Iran is always an important

risk factor for the propagation of infectious diseases, mainly from the eastern and western neighbors. The majority of these countries do not have High quality veterinary services for controlling animal diseases and common long borders and weaknesses in the border quarantine system facilitate the transportation of vertebrate and invertebrate host of BTV. Therefore, this situation can be an important risk factor for the spread and persistence of BTV in Iran. Some researchers (Azimi *et al*., 2008, 2011; Khezri and Bakhshesh, 2014) believe in trans-boundary virus between Iran and its neighboring countries as comparison of detected S7 gene from Iranian BTV strains indicated that there were two distinct clusters classified with BTV4 and BTV9/16 from Turkey (Azimi *et al*., 2008, 2011).

Hematophagous *Culicoides* insects are biological vectors that transmit BTV from infected to susceptible ruminants, and because BTV infection of ruminants is not contagious, the global distribution of BTV coincides with the distribution of competent *Culicoides* insect vectors and warm or hot climatic conditions. Thus, the virus exists in an extensive band that includes tropical, subtropical, and temperate regions of the world between latitudes of roughly 40° North and 35° South (Maclachlan and Osburn, 2006). So far, less than 1% of more than 1,400 *Culicoides* species described have been incriminated in the transmission of BTV, although relatively few species have been studied (Oryan *et al*., 2013). Species of *Culicoides* that transmit BTV differ amongst regions, *C. imicola* is the principal vector in Africa, the Middle East, most of south-east Asia and parts of south Europe, *C. soronensis* is the principal vector in North America and *C. brevitarsis* in Australia (Sperlova and Zendulkova, 2011; Wilson and Mellor, 2009). Because of its latitude (It lies between latitudes 24° and 40° N) and climate, Iran is considered a favorable country for presence and abundance of *Culicoides* vectors. Although *Culicoides* ssp. have been reported from Iran, there is no information on the *Culicoides* vectors of BTV in Iran (Abdigoudarzi, 2016).

Climate is a major risk factor because *Culicoides* require warmth and moisture for breeding and calm, warm, humid weather for feeding. A cold winter or a dry summer can markedly reduce vector numbers and risk for disease. Moisture may be in the form of rivers and streams or irrigation, but rainfall is the predominant influence; rainfall in the preceding months is a major determinant of infection. Ambient temperatures for survival of adult midges and larvae must be above a mean of 13° C (55° F) and range between 18° and 30° C (64° and 86° F) for optimal adult activity (Constable *et al*., 2017; Tabachnick, 2004). *Culicoides* populations can build up to high abundances under appropriate conditions, and adults can be transported by the wind for several kilometers within one night, resulting in rapid spread of the diseases they carry (Purse *et al*., 2008). Unfortunately, in recent years, climate change and global warming provided the opportunity for biting midges to have an extended period of activity and expanded the time intervals for BTV transmission. These changes lead to widespread and numerous epidemics of BTV around the world (Purse *et al*., 2005). According to the annual data of the Iran Meteorological Organization for Iran weather, there are both increasing and decreasing trends in annual rainfall in various regions, but temperature in most of the studied stations in recent years was increasing. So, these climate changes can influence the density of vector population and then the disease prevalence in Iran (Islamic Republic of Iran Meteorological Organization).

There are about 70,000,000 sheep and goats with 28 known breeds, which are reared by the villagers and nomadic tribes. Flocks of small ruminants are mainly managed under two different systems, namely, village and migratory (nomadic). Animals in both systems are mostly kept on natural grasslands and farmlands with little supplementary feeding and in a few cases, intensive systems of production are employed (Kamalzadeh *et al*., 2008), sheep and goat husbandry hygiene level (manure, pond, and stagnant water management), nutrition and animal welfare in village and migratory systems are less than in Intensive systems and the environmental conditions in village and migratory systems because of the presence of rivers, wet-lands such as the marshes, lakes, oasis and pools are suitable for the raise, survival and vectors activity. Therefore, graze based management can be a probable cause for the higher prevalence of disease in sheep and goats in Iran. Infection in pregnant ewes may lead to abortion, foetal mummification and the birth of weak calves with potential congenital defects (Sperlova and Zendulkova, 2011). The occurrence of high prevalent abortion in the domestic small ruminants of Iran has multifactorial etiologies. A survey on that 4625 aborted fetuses of sheep and goat flocks of Iran to detection viral and bacterial agents during 2002-2004, showed that 15.4% BTV were

identified as abortion related agents (Esmaeili *et al*., 2011). Results of this study revealed that there is a high seroprevalence of bluetongue infection among sheep and goat, so BTV can a crucial pathogen in sheep and goat abortion in Iran.

Cattle, while commonly infected in endemic and epizootic areas, rarely develop clinical disease So, cattle are important in transmission and acting as reservoirs for the BTV (Constable *et al*., 2017). At present, there are around 8,000,000 of three categories of cattle breeds in Iran: pure exotic (the Holstein is the most popular and dominating breed) that kept in industrial and semi-industrial farms whose hygienic level are higher than traditional breeding systems and crossbred of native and exotics and pure native breeds that reared in most of villages under a traditional system (Kamalzadeh *et al*., 2008). Based on our results, the seroprevalence of bluetongue among cattle was 3.3% (95% CI= 0.06–15.0) in Iran. that can be considered as a low rate in compared with some countries in the Middle East such as Turkey (17.4-88%) and Suadi Arabia (44.8%) (Celik and Sahin, 2018; Gür, 2008; Simsek *et al*., 2017; Yousef *et al*., 2012).

The results of this study showed Iranian camels have a high seroprevalence of BTV and are similar to those reported in Sudan 44.8% and Saudi Arabia 67% (Saeed, 2017; Yousef *et al*., 2012). This indicates that Iranian camels are an important reservoir of bluetongue virus and breeding them along with small ruminants in a traditional way can be a risk factor for the spread of the virus in sheep and goat population in the country (Mahzounieh *et al*., 2012).

The economic losses because of bluetongue are both direct (death, abortions, weight loss or reduced milk yield and meat efficiency) and, what is more important, indirect as a result of export restrictions for live animals, their semen and some products like fetal bovine serum. The costs of preventive and control measures should also be taken into account (Kyriakis *et al*., 2012; Sperlova and Zendulkova, 2011). Livestock is an important national resource in Iran. More than half of the rural population depends at least in part on livestock for their livelihood. Livestock plays a key role in the lives of the rural poor, generating employment and often providing some of their cash income (Kamalzadeh *et al*., 2008). The information on the annual cost of BT to the Iranian livestock industry isn't available, but it is estimated that the United States has an annual loss of $144 million because of the inability to trade with BTV-free countries (Constable *et al*., 2017).

Conclusions and Recommendations

The study highlights the endemicity of BT in farm animals of Iran and difference in seroprevalence across regions. In Iran, there is no defined control program for bluetongue. there is no vaccination against bluetongue disease in Iran and the exact number of circulating and dominant serotypes in Iran, is still unknown. In addition, there is no official attempt to control of *Culicoides* vectors in Iran. A well-defined control strategy for preventing and controlling BTV spread in Iran should be based on further studies on BT epidemiology especially in northern provinces and BTV serotypes, vector control to reduce the transmission, control of animal movement to reduce the spread to new areas and vaccination of sheep or susceptible species to reduce transmission and economical losses.

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Author's Contribution

The initial idea: MH and OM; Search and selection of final included studies: MH and OM; data analysis: MH; original draft preparation, writing, review and editing: MH and OM.

Conflict of interest

The authors have declared no conflict of interest.

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