Prevalent Infectious Causes of Abortion in the Ruminant Population in Iran- A Literature Review

Abstract

Abortion is one of the most crucial problems of ranchers in Iran, in different aspects, i.e. economic, animal healthcare or zoonotic. Each year the farm animal industry in Iran suffers from major economic losses due to abortion. Until now, some epizootological studies have been set up on infectious agents of ruminant abortion in Iran. However, there is no comprehensive information on the ruminant abortion status in Iran. We aimed at collecting all the available information on common infectious causes of abortion in ruminants in Iran to have a better picture of the situation in the country.

This review covers all of published documents in the main English and Persian-language databases on infectious agents of ruminants (cattle, sheep, goats, camels and buffalo) abortion in Iran from 1980 until May, 2024.

Although ruminant abortion in Iran has multifactorial etiologies, but the present study could represent infectious diseases as a serious risk factor in predisposing the ruminants to abortion. Important putative infectious agents that cause abortion in sheep and goats include toxoplasmosis, chlamydiosis, brucellosis and coxiellosis and in cattle include neosporosis, BVDV and BoHV-1.

According to our result, a well-defined control strategy for preventing and controlling infectious abortion in Iran should be based on further epidemiological studies on cause of abortion, accurate records keeping, perform laboratory analysis, control of animal trafficking from neighboring countries and from one region to another within the country, employing good biosecurity practices that inhibit the introduction and spread of infectious causes of abortion and using vaccination programs.

Key words: Abortion, Infectious Agents, Ruminants, Iran

1. Context

Abortion is one of the most important problems of livestock production worldwide, causing severe economic losses including loss of fetuses, uterine infections, increased calving/lambing/kidding interval and infertility, costs for additional inseminations to get cows or heifers pregnant, veterinary cost, reduce milk production, diet costs through the extra days open, culling or death of animals, loss of potential to produce calf/lam/kid replacements, the costs of increased time and labor incurred in managing an abortion outbreak and the cost of human disease given that many of the agents of abortion are zoonotic (1–3).

Abortive agents in farm animals are so various and complex and its epidemiological patterns diff er greatly between geographical areas depending on climate, population density, housing and breeding systems, introduction of new infectious agents, control measures like vaccination and processing technologies. Agents responsible for livestock abortion can be classified as infectious and non-infectious. Infectious agents are the leading causes of abortion in ruminant in comparison to non-infectious agents and are often infectious to humans (3–5). The main zoonotic etiological agents are *Brucella*, *Salmonella*, *Campylobacter*, *Leptospira* and *Listeria* species, *Chlamydia abortus*, *Coxiella burnetii* and *Toxoplasma gondii* that could transmit from animals to humans when handling infected animals, during obstetrical acts when giving birth or after that, sometimes when milking abortive females, also after drinking infected or contaminated milk (6).

Iran has approximately 70 million head of cattle, sheep, goats, camels and buffalo; its ruminant industry accounts for approximately 11% of the Gross Domestic Product. Infectious abortion is one of the most important diseases in ruminant production in Iran economically from losses in both production and veterinary services, and from zoonotic risk particularly to the ranchers and veterinarians.

Since the 1940s, various epizootological studies have been set up on infectious agents of ruminant abortion across different states and time periods in Iran, However, there is no comprehensive information on the ruminant abortion situation in Iran.

Our aim is to provide a clearer understanding of the situation in the country. Specifically, we seek to identify the key pathogens involved, their incidence and/or prevalence, their impact on ruminant production, the practices used in their prevention and control, and finally, their impact on the health of humans who rely on ruminants and their products in Iran.

2. Data Acquisition

2.1. The study area: Iran

The literature reviewed was limited to studies conducted in Iran. The country is located in the Middle East, western Asia between latitudes 24–40 N, and longitudes 44–64 E. Iran shares borders with Armenia, the Azeri exclave of Nakhichevan, and the Republic of Azerbaijan, Turkmenistan, Afghanistan, Pakistan, Iraq and Turkey. It has an area of 1,648,195 km^2 and with a population of over seventy million people. Iran's climate varies from arid and semi-arid, to subtropical along the Caspian coast and the northern forests and ranging 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 in the north (Fig. 1).

2.2. Search criteria

For gathering information on infectious agents of ruminant (cattle, sheep, goats, camels and buffalo) abortion in Iran, articles published from 1980 until May, 2024 in both English and Farsi language were searched in eight databases were included: five English databases (PubMed, Google Scholar, Science Direct, Web of Science and Scopus) and three Persian databases (Magiran, Irandoc and the Scientific Information Database [SID]). We also searched dissertations and all abstract books of scientific congresses in Iran from 2000 to May, 2024. In order to avoid missing any articles, the citations of the included articles were reviewed to identify other relevant studies. The search terms which were used alone and/or combined included ‘‘Brucellosis,’’ ‘‘*Brucella abortus*,’’ ‘‘*Brucella melitensis*,’’ ‘‘*Brucella ovis*,’’ ‘‘Listeriosis,’’ ‘‘*Listeria monocytogenes*,’’ ‘‘*Listeriosis ivanovii*,’’ ‘‘Salmonellosis,’’ ‘‘*Salmonella Abortus-ovis*,’’ ‘‘Vibriosis/Campylobacteriosis,’’ ‘‘*Campylobacter jejuni* subsp. *jejuni*,’’ ‘‘*Campylobacter fetus* subsp. *fetus*,’’ ‘‘*Campylobacter fetus* subsp. *venerealis*,’’ ‘‘Leptospirosis,’’ ‘‘*Leptospira interrogans*,’’ ‘‘Chlamydiosis,’’ ‘‘*Chlamydia abortus*,’’ ‘‘Coxiellosis,’’ ‘‘*Coxiella burnetii*,’’ ‘‘*Escherichia coli*,’’ ‘‘*Streptococcus* spp.,’’ ‘‘*Staphylococcus* spp.,’’ ‘‘*Bacillus* spp.,’’ ‘‘*Pasteurella multocida*,’’ ‘‘*Mannheimia hemolytica*,’’ ‘‘*Haemophilus somnus*,’’ ‘‘*Arcanobacterium pyogenes*,’’ ‘‘*Yersinia pseudotuberculosis*,’’ ‘‘*Pseudomonas* spp.,’’ ‘‘*Mycoplasma mycoides*,’’ ‘‘*Mycoplasma agalactiae*,’’ ‘‘*Ureaplasma diversum*,’’ ‘‘Neosporosis,’’ ‘‘*Neospora caninum*,’’ ‘‘Toxoplasmosis,’’ ‘‘*Toxoplasma gondii*,’’ ‘‘Trypanosomosis,’’ ‘‘*Trypanosoma evansi*,’’ ‘‘Tritrichomonasis,’’ ‘‘*Tritrichomonas foetus*,’’ ‘‘Sarcocystis,’’ ‘‘Bovine viral diarrhea virus,’’ ‘‘Bovine herpesvirus-1,’’ ‘‘Bluetongue virus,’’ ‘‘Border Disease virus,’’ ‘‘Caprine herpesvirus type 1,’’ ‘‘Bunya virus,’’ ‘‘Rift Valley fever,’’ ‘‘Akabane virus,’’ ‘‘Cache Valley virus,’’ ‘‘Nairobi Sheep Disease Virus,’’ ‘‘Schmallenberg,’’ ‘‘Aspergillusis,’’ ‘‘*Aspergillus fumigatus*,’’ ‘‘*Absidia* spp.,’’ ‘‘*Mucor* spp.’’ ‘‘*Rhizopus* spp.’’ ‘‘*Candida* spp.,’’ ‘‘abortion,’’ ‘‘epidemiology,’’ ‘‘animals,’’ ‘‘ruminant,’’ ‘‘cattle,’’ ‘‘bovine,’’ ‘‘sheep,’’ ‘‘ovine,’’ ‘‘goat,’’ ‘‘caprine,’’ ‘‘camel,’’ ‘‘buffalo’’ and ‘‘Iran.’’ All listed terms were also searched in Persian. Exclusion criteria were articles that did not contain complete information about infectious agents of abortion.

3. Results

3.1. Literature Reviewed

After putting off duplications based on title and abstract, articles which describe the infectious causes of abortion in aborted fetuses of ruminants (cattle, sheep, goats, camels and buffalo) in Iran were selected. Based on sampling strategy, studies with non-random sampling samples from one herd because of creating bias were excluded from this research. Furthermore, the studies with small sample size (<10) were excluded from the review. Most of the reports were PCR-based studies focusing on aborted sheep fetuses in Iran, and no studies were found concerning buffalo. As shown in Table 1, we classified infectious causes of abortion in Iran into bacteria, viruses, protozoa and fungi. We estimated the incidence of abortion caused by these agents as low, medium or high based on our literature review. Further details on PCR-based studies are summarized in Tables 2 through 8, categorized by animal group, study area, and the number and type of samples.

3.2. Status of abortion in livestock in Iran

Abortions in livestock may be induced by numerous factors, with a wide range of agents, either infectious or noninfectious that may occur sporadically or as enzootic outbreaks (7). Infectious agents are more commonly associated with abortion in domestic animals compared to non-infectious causes, and some infectious agents are zoonotic, which can be transmitted from animals to humans and have significant effects on human health (6).

The prevalence of abortion varies according to production systems and locations. In healthy flocks and herds of ewes and does, the visibly aborting rate is usually less than 2% (4). Noninfectious abortions related to traumatism, pregnancy toxaemia, vitamin E/Se deficiency, stressful handling, overcrowding, or even consuming toxic plants rarely result in more than 2% of the flock aborting, and when the percentage is higher, it is highly likely that an infectious cause of abortion (4,8).

The incidence of abortion of more than 2% or a clustering of abortions within a short time (eg, 2 weeks) or a given location (eg, pen or farm) should be viewed seriously, efforts should be made to determine the causes and measures should be taken to control abortion (4). Unfortunately, there's no official data on the incidence of abortion within the country. However, the incidence of abortion could also be absolutely various in different areas on the idea of the wide spectrum of climate conditions, different husbandry systems, species and breed variation in Iran.

It has been reported that outbreaks of abortion are annually observed in sheep and goat herds in different parts of Iran. However, lack of reliable statistics on incidence of abortion and proportion of lambs and kids stillborn, has contributed to the neglect of control this disease in these species (9). A cross-sectional survey on 757 sheep flocks in Iran revealed that 213 (28.1%) had an abortion rate below 2%, the remaining 544 (71.8%) flocks had pathological abortion rates (> 2%), and infectious agents were diagnosed as a cause of abortion in 287 flocks (37.9%) (10).

According to the definition of abortion as a loss of the fetus between the age of 60 and 260 days of pregnancy, the overall cattle abortion rate from years 2004 to 2014 using calving records gathered from herds of different regions of Iran was 15.5% (11.2-18.7%). The highest incidence abortion was found for second parity cows. The highest and lowest rates of abortion happened in the mild and cold climate, respectively. Furthermore, the average abortion rate incidence was highest in the spring and lowest in the autumn (11).

There are insufficient studies on abortion rate in other ruminants in Iran (12). In 2014, an outbreak of abortion storm in camel herds was documented in Qom province, where 494 out of 846 (58.4%) pregnant camels and 45 out of 35 herds (77.8%) were aborted. The rate of abortion in herds was from 14 to 100% (13).

3.3. Economic impact of abortion on production in Iran

According to the latest report (2019) of the Ministry of Agriculture of Iran, the total number of sheep, goats and cattle in various regions of the country is approximately 44 million, 17 million, and 8 million animals, respectively. Iran is also home to more than 220,000 buffalo (Azeri breed) and two camel species: *C. dromedarius* and *C. bactrianus* with the populations of approximately 190,000 and around 100-300, respectively. The annual milk and meat production of cows and small ruminants is estimated to be approximately 10,000 and 500 and 460 and 360 (× 1000 tons) , respectively (14).

The information on the annual cost of abortion to the Iranian sheep and goat industry isn't available but we can consider huge financial losses related to both direct and indirect costs. Some of these indirect costs are associated with an increase in lambing/kidding intervals, fewer available replacement lambs, increased time to marketable weight and increased costs of production resulting from birth of small, weak lambs/kids and decreased growth rates and an increase in veterinary treatments.

Abortion and reproductive failure are the most prevalent reason of culling cows in Iran (15). Each abortion in cattle costs an Iranian producer about 810,000 to 12,760,000 Rials (approximately 82–1302 US$), depending on factors such as pregnancy rate, feed and milk prices, milk production, days in milk, the time of insemination after parturition, semen costs, insemination time, and labor costs (16).

3.4. Health management procedures for controlling infectious abortion in Iran

In Iran, the majority of livestock is still kept by small holders under traditional breeding farms in two different systems, namely village and migratory (nomadic) and animals are in direct contact especially with shepherd and stray dogs. In a few cases especially about cattle breeding, intensive systems of production are employed having higher hygiene level, nutrition and animal welfare (Kamalzadeh et al., 2008).

Except a defined control program against brucellosis as a priority disease in the Middle East has been setup since 1949, there is no national program for the control of abortion within the Iranian Veterinary Organization and measures are instituted at the herd level at the discretion of the individual producer.

Following is some of the major problems for abortion control in Iran:

1- Traditional breeding system: in tradition breeding system, health and reproduction complications are high due to geographical, economic and cultural situations or lack of sufficient information on farm animal husbandry and stress factors are common in these systems. Therefore, herds and flocks suffer from weaknesses in actions such as maintenance of the general health and immune function of animals by providing a balanced feed and clean water, improving the hygiene level by isolation of purchased livestock before entering the herd, keeping aborted animals separate from other livestock, complete disposal of the aborted material with which shepherd dogs or other stray animals are fed as a routine way in Iran, make the life cycle of *Toxoplasma gondii* and *Neospora caninum* as important protozoal infections of abortion survive, using vaccination programs and a good record-keeping including abortion events, vaccination, nutrition, possible exposure to toxic or teratogenic plants or drugs and possible environmental factors such as extreme heat or stress which can help to focus the diagnostic investigation.

2- Animal movement control: Weaknesses in animal movement control within the country especially because of the existence of nomadic and semi-nomadic conditions.

3- Geographic situation: of Iran can be an important risk factor for spread and persistency of contagious diseases from the eastern and western neighbors such as Iraq, Pakistan & Afghanistan. The majority of these countries do not have high quality veterinary services for controlling animal diseases and there are weaknesses in the border quarantine system and animal trafficking from these countries into Iran.

4- Diagnosis and Treatment Limitation: The high cost of laboratory work to aid in the diagnosis of abortion and control and treatment measurements also compounds the problem in Iran. On the other hand, laboratories only conduct routine aerobic cultures on blood agar and MacConkey agar, so in this way, many factors remain hidden from the view.

3.5. Infectious causes of livestock abortion in Iran

3.5.1. Bacterial Infections

3.5.1.1. Brucellosis

Brucellosis is one of the most important zoonosis that cause stillbirth, abortion, infertility and reducing the efficiency of milk and meat production in livestock. Brucellosis in cattle is most commonly caused by *B. abortus* although *B. melitensis* can occasionally be involved. *B. melitensis*, is the cause of brucellosis in sheep and goats but, *B. abortus* infection can also occurs in these animals (17–19).

Brucellosis in the cattle population of Iran was diagnosed with *B. abortus* isolation from an aborted fetus in 1944 (20). Up to now, *B. abortus* biovar 1, 2, 3, 4, 5 and 9 and *B. melitensis* biovar 1, 2 and 3 have been identified in Iranian cattle, however *B. abortus* biovar 3 is as the dominant one (21). Prevalence of brucellosis among industrial and semi-industrial dairy cattle calculated as 0.3% (22). The national control plan for cattle brucellosis includes vaccination as well as test and slaughter. Vaccination programs were begun in 1949 using the Strain 19 vaccine but since (year) vaccination of adult cows and 4 - 12-month-old female calves are done using a reduced and full dose RB51 vaccine, respectively. Test and slaughter are based on serological screening using RBPT and confirming positive results using STAT and 2ME tests, of all industrial farms. In rural and nomadic areas control measures are implemented following outbreaks of animal or human brucellosis and villages which sell milk to milk processing plants (22,23). There are potential hazards related to the use of the Rev.1 vaccine in the national control programs, as cattle and small ruminant are kept close together in traditional farms and sheep and goats vaccination (Rev.1) can be a source of *Brucella* abortion in cattle (24). Furthermore, there are reports on abortion in cows with *B. abortus* vaccine strain RB51 in Iran (25,26).

Brucellosis in small ruminant has been studied since 1949, when the *B. melitensis* was first isolated from milk of an aborted goat (23). The prevalence of brucellosis among small ruminants in Iran calculated as 2.1% (27). According to the results of some reports; *B. melitensis* biovar 1 is endemic and widely spread in Iranian sheep and goats but also *B. melitensis* biovar 2 and 3 and *B. abortus* biovar 3 has been found (21). Vaccination of sheep and goats was started in 1963 using the full dose Rev.1 vaccine production in Razi Institute in Iran. In 2003, adult vaccination with a reduced dose of Rev-1 vaccine was substituted for the full dose, and test and slaughterwas eliminated except in breeding centers, industrial farms and areas with abortion outbreaks (23,27). Some reports revealed that reduced dose of Rev-1 vaccine was implicated as the cause of abortion in some regions of Iran and was isolated from aborted fetus of small ruminants (28)

According to the serological tests, the prevalence of brucellosis in Iranian buffalo and camels is between 1.5 to 20.5% and 1.3 to 9.3% respectively (21,29).

Based on bacterial culture studies conducted in 1980s in Iran, infection rate of brucellosis in aborted fetuses of small ruminants and cattle was 25.3% (426/1680) and 43.5% (875/2009) respectively (30). Recent studies showed in table 2 have revealed that the rate of abortion in sheep and cattle range from 3.5 to 19.2% and 4.5 to 7.8% in different provinces respectively, indicate that animal vaccination have had a noticeable effect for controlling the infection in Iran.

3.5.1.2. Listeriosis

Listeria monocytogenes is an important zoonotic food born pathogen with the potential to cause various clinical forms in ruminants, ranging from mastitis, keratoconjunctivitis, uveitis, gastroenteritis, encephalitis, neonatal septicaemia, premature birth or abortion (31,32).

There are few reports of listeriosis- related abortion in ruminants in Iran. In two studies of aborted small ruminant fetuses submitted to Iranian veterinary diagnostic laboratories, *L. monocytogenes* was found in 0.0-2.8% of examined ovine and caprine aborted fetuses (33,34).

3.5.1.3. Salmonellosis

Salmonellosis is an infectious zoonotic disease caused by *Salmonella* ssp. which can cause foodborn poisoning in human through animal products, and can induce abortion and mortality in the newborn ruminants (35,36).

Outbreaks of salmonellosis in sheep herds associated with mortalities and abortions have been documented in Iran. Some surveys using bacterial culture and PCR, have revealed that the rate of abortion in ewes due to *S. abortus ovis* range from 1.3 to 33% in different provinces (37–39). In the only report on *Salmonella* outbreak in Iranian camels, Muhammadi and Mosleh (2017) examined the gallbladder contents and amniotic fluids of 10 aborted dromedary fetuses in Khorasan Razavi and isolated the pathogen from 2 cases (40).

3.5.1.4. Campylobacteriosis

Campylobacter species are significant zoonotic causes of bacterial food-borne infection and in ruminants *Campylobacter fetus* subsp. *fetus*, *venerealis* and *jejuni* are the most important species related to lowered fertility and abortion (41–43).

Infection with *C. fetus* infection as an abortive agent was confirmed in numerous abortion outbreaks in sheep population in Iran (44,45). Based on PCR studies showed in table 3, the prevalence of campylobacteriosis infection in ovine aborted fetuses is between 3.5% to 10.6% (Table 3). Based on bacterial culture and PCR studies conducted on cattle population in Iran, infection rate of campylobacteriosis in aborted fetuses was 4.2% (50/1186) and 3.9% (3/76) respectively (26,46).

3.5.1.5. Leptospirosis

Leptospirosis is an important zoonotic disease of mammals which is caused by pathogenic spirochaetes of the species *L. interrogans.* Cattle are relatively susceptible to clinical infection, resulting in production losses including reduced milk yield, reproductive failure, abortions, premature birth or stillbirth (47,48).

In Iran, leptospirosis seroprevalence in unvaccinated cattle, sheep and goat population at animal level is 25.6% (95% CI= 19.8-32.3%), 17.4% (95% CI= 12.4-23.8%) and 14% (95% CI= 11.9-17.5%) respectively and the most prevalent serovars are *grippotyphosa, pomona,* and *canicola* (49). Based on the PCR studies, *Leptospira* DNA has been detected up to 21.0% and 8.6% of bovine and ovine aborted fetuses in Iran, respectively (Table 4).

3.5.1.6. Chlamydiosis

Chlamydia abortus as zoonotic pathogen, (previously known as *Chlamydophila abortus* and *Chlamydia psittaci* biotype 1/serotype 1) is a common cause of abortion in ruminants specially in sheep and goats (50–52).

Few surveys have been carried out on the seroepidemiology of chlamydiosis among ruminants in Iran. In a study in 2011 which investigated the presence of *C. abortus* in sheep and goats, Esmaeili *et al*., found 25.6% seropositive in the individual level and 81.4% in unvaccinated flocks in seven provinces of Iran (53). Furthermore, a cross-sectional was conducted study on 834 vaginal and ocular swabs collected from 83 flocks of different regions of Iran, DNA of *C. abortus* was detected in 117 samples from 504 sheep (23.2%) and 84 from 330 goats (25.5%) (54). Another study, reported 48.4% prevalence of *C. abortus* antibodies in aborted cattle in some farms around Tehran province (55). According to listed studies in table 5, *C. abortus* infection in farm animal aborted fetuses in Iran is considerable, up to 52% and 22.0% in sheep and goats respectively, therefore it can be a major role in abortion and economic losses in small ruminants breeding.

3.5.1.7. Coxiellosis (Q Fever)

Coxiellosis or Q fever is a highly contagious zoonotic disease caused by *Coxiella burnetii*. This bacterium is a cause of sporadic abortion or abortion storms in sheep and goats but only uncommonly associated with sporadic abortion in cattle (56,57)

Q fever is an endemic disease in Iran, which is mostly reported in human and domestic animals from almost all the provinces of the country (58). The individual prevalence of *C. burnetii* antibodies in unvaccinated sheep, goat and cattle in Iran is 24.6% (95% CI= 19.8–29.5%), 31.9% (95% CI= 20.9–42.9%), 13.3% (95% CI= 2.9–23.6%), respectively (59). PCR-based

studies indicated that the *C. burnetii* has a crucial role in abortion cases of small ruminants (0.0-21.8%) and cattle (21.7-25%) in Iran (Table 6).

3.5.1.8. Other, less common bacteria

Several other bacteria have been isolated from aborting sheep and goats. These bacteria cause sporadic, individual animal problems and do not represent a serious flock problem. Mechanistically, most infections are associated with an initial septicemia in the dam followed by localization of the bacteria to the uterine caruncle and infection of the placental cotyledons (60). Bacteria including *Escherichia coli*, *Staphylococcus* spp., *Streptococcus* spp., *Bacillus* spp., *Mannheimia haemolytica*, *Mycoplasma agalactiae* and *Erysipelothrix rhusiopathiae* have been isolated from aborted fetuses of ruminants in Iran (33,34,61–67).

3.5.2. Protozoal Infections

3.5.2.1. Toxoplasmosis

The protozoan *Toxoplasma gondii* as the agent of toxoplasmosis, is an important zoonotic pathogen that causes abortion, mummification, stillbirth, and birth of weak newborns in sheep and goats (68,69). Cats and other Felidae as definitive hosts play an important role in the epidemiology of toxoplasmosis. These hosts can be infected when ingest food contaminated by oocysts or containing tachyzoites or tissue cysts from infected mice. The cats excrete oocysts for up to 14 days after infection and sporadically after that. Sheep and goats become infected by ingesting contaminated food or pasture with environmentally resistant oocysts excreted in cats' feces (70–72).

Stray cats are probably the main source of *T. gondii* infection in Iran. The seroprevalence rate of toxoplasmosis in cats in Iran is considerable (33.6% (95% CI= 22–46.4)), and this high infection rate of final hosts can be considered a potential threat to human and animals health due to high contamination of the environment with oocysts (73). The overall individual prevalence rate of toxoplasmosis in Iran was estimated to be 31% (95% CI= 26.0 35.2%) in sheep, 27 % (95% CI= 14.0- 42.5%) in goats and 18.1% (95% CI= 9.9-28.2%) in cattle (74,75). Based on PCR studies showed in table 7, toxoplasmosis has a major role in ovine abortion up to 68.2% of ovine fetuses positive in Iran. Occurrence of an outbreak of ovine congenital toxoplasmosis was reported in 2010-11 in Khorasan Razavi province, Iran. The flock consisted of 240 ewes with no abortion history. During one month, 65 lambs were aborted at late pregnancy period, 12 lambs were born weak and 4 of them died 4 to 5 days after birth and eight lambs were too weak and with motion disabilities (76)

3.5.2.2. Neosporosis

Neospora caninum is considered as a significant cause of bovine abortion in most of the major cattle-producing areas of the world. Domestic dogs and other species of canines are definitive hosts for *N. caninum* and after ingestion of *N. caninum*-infected body tissues from intermediate hosts, they can transiently shed oocysts (70,77). Intermediate hosts become infected either via ingestion of contaminated food and water with oocysts (horizontal transmission), or via trans-placental transmission from infected dams to their offspring (vertical transmission). Healthy calves which have been prenatally infected, remain persistently infected and can pass the infection to their own calves (70,78).

The overall seroprevalence of *N. caninum* in cattle population in Iran is estimated 23.6% (95% CI= 19.8-27.9%) based on a meta-analyses study (79). Also documented studies in Iran show that the presence of farm dogs can be a risk factor for *N. caninum* infection in dairy farms with the infection rate between 0 to 54.6 % (80). *N. caninum* infection in dairy cattle in Iran can be an important agent of abortion. Reports on the prevalence of *N. caninum* infection in cattle indicate that 11.0–45.0% of the PCR-examined aborted fetuses had positive (Table 8). *N. caninum* infection were also reported 1.1–6.8% in sheep, 6.2-10.8 % in goats, 19.2-55.9% in water buffalo and 3.2–27.0% in camels in Iran (80). Although, *N. caninum* occasionally causes clinical infections in sheep and goats. Several research projects on neosporosis abortion in sheep had been carried out in Iran indicating *N. caninum* may act as a causative agent of abortion in sheep, as DNA from *N. caninum* was detected up to 15.6% of samples derivate from aborted fetuses (Table 8).

3.5.2.3. Trypanosomosis

The most important protozoal disease of camels is trypanosomosis (also known as surra), caused by *Trypanosoma evansi* and is now considered as a zoonotic disease. The disease in camel is characterized by recurrent fever, anemia, emaciation and diarrhea, atrophy of the thigh muscles, lacrimation, corneal opacity, edema, abortions, premature births and death (81). The disease was confirmed in Iranian camels in 1935 and since then numerous studies on the prevalence of trypanosomosis in dromedary camels reported range from 0 to 19.5% (20,82). Abortion associated with outbreaks of trypanosomosis have been documented in dromedary herds of Iran (83); however, there is only one report on the role of *T. evansi* infection in camel abortion (84). In this PCR study, 41 out of 244 (16.8%) abomasal contents of aborted fetuses were collected from eastern provinces, were infected with *T. evansi*.

3.5.3. Viral Infections

3.5.3.1. Bovine viral diarrhea virus

Bovine viral diarrhoea virus (BVDV), a member of Pestivirus genus and Flaviviridae family, is one of the most important viral pathogens of cattle and responsible for major economic losses in dairy industries worldwide (85). BVDV causes multiple clinical syndromes including bovine viral diarrhoea, mucosal disease, respiratory problems, reproductive complications including embryonic resorption, abortion, stillbirth, infertility, congenital defects or the birth of persistently infected (PI) calves, which are the principal reservoir of the virus in nature (86,87).

The prevalence of BVDV in unvaccinated bovine in Iran has been reported on the basis of the detection of antibody against BVDV a range of 20-90% (88). Although the exact prevalence of BVDV-induced abortion in cattle is not well-documented in Iran, several PCR studies have revealed that the rate of BVD-infected aborted fetuses range from 20.3 to 25.2% in different provinces (89,90).

3.5.3.2. Bovine herpesvirus type 1 (BoHV-1)

Infection with Bovine herpesvirus type 1 (BoHV-1) can lead to several clinical syndromes including inflammatory reactions in both respiratory (Infectious Bovine Rhinotracheitis) and genital tracts (infectious pustular vulvovaginitis/balanopostitis), conjunctivitis, encephalitis, abortion, infertility, mastitis, enteritis, dermatitis and also a systemic form affecting visceral organs in newborn calves (91–93).

The total seroprevalence of BoHV-1 in unvaccinated cattle in Iran is 402% (95% CI= 32.3–48.6) at the animal level and 75.5% (95% CI= 63.9–84.2), at the herd level (Hassani M & Hemmatzadeh F, unpublished material). Some investigations using PCR reported the prevalence of abortion caused by BHV-1 in bovine is between 6.8 to 13.3% which indicate BHV-1 can be a considerable aborted factor in cattle population in Iran (90,94).

3.5.3.3. Bluetongue virus

Bluetongue is an infectious, non-contagious disease caused by an Orbivirus of the family Reoviridae which is mainly transmitted by insects. It can cause erosions in mouth, nasal mucosa, limbs as well as abortion in affected animals. In the pregnant ewes may lead to abortion, foetal mummification and the birth of weak lambs with potential congenital defects (95,96). The infection is widespread in Iran with high seroprevalence among unvaccinated sheep (50.4% (95% CI= 43.5–57.2%)) and goat (79.9% (95% CI= 70.7–85.8%)) at animal level (97). In the only study conducted on the occurrence of abortion owing to bluetongue in Iran, Mahzounieh *et al.*, (2014) detected no positive cases in 50 aborted lambs using RT-PCR in Chaharmahal va Bakhtiari and Isfahan provinces (98).

3.5.3.4. Border Disease virus

Border disease is caused by border disease virus (BDV), a pestivirus which belongs to the Flaviviridae family and is closely related to Bovine Virus Diarrhoea Virus (BVDV). The disease is characterized by abortions, congenital abnormalities, and stillbirths, the birth of small weak lambs and persistent infections of the off spring in in sheep and goats flocks (99,100). Until now, some serological investigations have been carried out on the presence of BDV antibodies in different regions of Iran that have shown the individual prevalence of 3.2-79.5% in sheep and 64.0-70.9% in goats (Hassani M, unpublished material). However, there are only one RT-PCR studies on BDV as an aborted agent in sheep from Iran. Mokhtari and Manshoori (2017) investigated the role of this viral infection in sheep abortion in Chaharmahal va Bakhtiari province and determined 9 (9.0%) of 100 samples were BDV positive (101).

3.5.3.5. Bunya virus

A number of Bunya virus infections are potentially teratogenic and abortive in ruminants including Akabane virus, Cache Valley virus, Rift Valley fever virus, Nairobi Sheep Disease Virus and Schmallenberg virus. In Iran, results of some surveys revealed the presence of Akabane virus (102,103), Rift Valley fever virus (104) and Schmallenberg virus (105) in ruminants, but none of these viruses were detected in aborted cases (106,107).

3.5.4. Fungal Infections

Mycotic abortions are normally sporadic, although in some herds the incidence may be as high as 5–10%. The majority of mycotic abortions in cattle are caused by *Aspergillus fumigatus*. Infections by other *Aspergillus* spp., *Absidia* spp., *Mucor* spp., *Rhizopus* spp. and *Candida* spp. occur less frequently (60,108).

There are not enough studies about the mycotic abortion in Iran. Vandyousefi and Zoghi (1988) isolated mycotic agents, from 50.5% (60/119) samples of bovine and ovine aborted fetuses, while no other infection agents were found on microbiologic examination (109). Esmaeili *et al*. (2022) by mycologic examination of abomasal contents of ovine aborted fetuses were collected from various parts of Iran, revealed the contamination rate of 1.5% at flock level (10).

4. Conclusion

The present work reflects the current state of knowledge on the infectious agents of ruminant abortion in Iran. However, this knowledge may not be exhaustive, as it relies on available clinical and scientific reports, supplemented by the unpublished experiences of the authors in areas where data is scarce. Other infectious agents may be present in Iran since they may not have been detected so far and included in published reports, for various reasons. This information would be helpful to open new opportunities for research on the eradication and control of the causative agents of abortion in ruminants.

Although occurrence of abortion in the ruminants in Iran has multifactorial etiologies, but the present study could represent infectious diseases as a major risk factor in predisposing the farm animals to abortion. Important putative infectious agents that cause abortion in sheep and goats include toxoplasmosis, chlamydiosis, brucellosis and coxiellosis in cattle include neosporosis, BVDV and BoHV-1.

Several of the pathogens associated with in ruminant are also zoonoses. So regardless of whether there is a perceived abortion incidence in the in flock or herd, pregnant women should be advised not to have contact with animals or with dirty work wear from the ranching environment.

According to our findings, a well-defined control strategy for preventing and controlling infectious abortion in Iran should be based on further epidemiological studies on cause of abortion, accurate records keeping, perform laboratory analysis, control of animal trafficking from neighboring countries and from one region to another within the country, employing good biosecurity practices that inhibit the introduction and spread of infectious causes of abortion and using vaccination programs.

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Authors' Contribution

Conception and research design: MH. Collection of data: MH and SA. Supervising and writing the draft of the manuscript: MH. All authors contributed to helpful discussions and approved the final manuscript.

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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Fig. 1 The map of Iran with different climate regions (Iran-climate.png.). This figure is shared under a CCBY 3.0 Share-Alike 3.0 Unported license. https://creativecommons.org/licenses/by-sa/3.0/deed.en.

Table 1. Infectious causes of abortion, potential zoonosis and incidence in ruminant population in Iran.

Pathogen agent	Potential zoonosis	Cattle	Sheep and goat
Brucella spp.	Yes	Low	High
Listeria monocytogenes	Yes	Low	Low
Salmonella spp.	Yes	Low	Low
Campylobacter spp.	Yes	Low	Low
Leptospira spp.	Yes	Moderate	Low
Chlamydia abortus	Yes	Low	High
Coxiella burnetii	Yes	Low	Moderate
Other bacteria	Yes	Low	Low
Toxopllasma gondii	Yes	Low	High
Neospora caninum	Yes	High	Low
Bovine viral diarrhea virus	No	High	-
Bovine herpesvirus1	No	Moderate	-
Bluetongue virus	No	-	Low
Border disease virus	No	-	Low
Fungal	Yes	Low	Low

Table 2. Infection rate of brucellosis in aborted fetuses of ruminants from different regions of Iran based on polymerase chain reaction (PCR).

Reference	Group	Study area	Aborted fetus sample type	No. of samples	species: No. of positive (%)
Mohammadi, 2016	Sheep	Golestan	Abomasal contents	57	*B. melitensis*: 10 (17.5)
Mahdavi Roshan et al., 2018	Sheep	Sistan va Baluchistan	Abomasal contents & spleen	78	*B. melitensis*: 15 (19.2)
Mahzounieh et al., 2019	Sheep	Different regions	Abomasal contents	98	*B. melitensis*: 15 (15.3)
Amouei et al., 2019	Sheep	Mazandaran	Abomasal contents	57	*B. melitensis*: 2 (3.5)
Hamali et al., 2013	Cattle	East Azerbaijan	Different tissues	76	*B. abortus.*: 6 (7.8)
Nemati et al., 2019	Cattle	Golestan & Razavi Khorasan	Different tissues	22	*B. abortus.*: 1 (4.5)

Table 3. Infection rate of campylobacterosis in aborted fetuses of ruminants from different regions of Iran based on polymerase chain reaction (PCR).

Reference	Group	Study area	Aborted fetus sample type	No. of samples	species: No. of positive (%)
Fallah et al., 2014	Sheep	East Azerbaijan	Different tissues & placenta	132	*C. jejuni*: 2 (1.5) *C. fetus fetus*: 12 (9.1)
Kabiri et al., 2016	Sheep	Different regions	Abomasal contents	98	*C. fetus*: 5 (5.1)
Mohammadi, 2016	Sheep	Golestan	Abomasal contents	57	*C. fetus*: 2 (3.5)
Hossein Abadi et al., 2018	Sheep	Sistan va Baluchistan	Abomasal contents & spleen	78	*C. fetus*: 6 (7.7)
Malekadeh Arasteh, 2021	Sheep	Khorasan Razavi	Liver	91	*C. fetus*: 6 (6.6)
Hamali et al., 2011	Cattle	East Azerbaijan	Different tissues & placenta	76	*C. fetus fetus*: 0 (0.0) *C. fetus venerealis*: 3 (3.9)

Table 4. Infection rate of leptospirosis in aborted fetuses of ruminants from different regions of Iran based on polymerase chain reaction (PCR).

Reference	Group	Study area	Aborted fetal sample type	No. of sample	No. of positive (%)
Badii et al., 2010	Cattle	Tehran	Different tissues	251	32 (12.8)
Hamali et al., 2013	Cattle	East Azerbaijan	Different tissues	76	16 (21.0)
Kaveh et al., 2017	Cattle	Qazvin	Different tissues	128	18 (14.1)
Froutani et al., 2014	Sheep	East Azerbaijan	Different tissues	70	6 (8.6)
Kabiri et al., 2016	Sheep	Different regions	Abomasal contents	98	0 (0.0)

Table 5. Infection rate of *Chlamydia abortus* in aborted fetuses of ruminants from different regions of Iran based on polymerase chain reaction (PCR).

Reference	Group	Study area	Aborted fetal sample type	No. of sample	No. of positive (%)
Mahzounieh & Pourahmad, 2014	Sheep	Charmahal va Bakhtiari	Abomasal contents	48	25 (52.1)
Ebadi et al., 2015	Sheep	Alborze	Abomasal contents	100	37 (37.0)
Mohammadi, 2016	Sheep	Golestan	Abomasal contents	57	0 (0.0)
Alem et al., 2017	Sheep	East Azerbaijan	Different tissues & placenta	50	13 (26.0)
Heidari et al., 2018	Sheep	Fars	Abomasal contents	183	15 (8.2)
Hosein Abadi et al., 2019	Sheep	Sistan va Bluchestan	Abomasal contents & spleen	78	0 (0.0)
(M Mahzounieh et al., 2019	Sheep	Different regions	Abomasal contents	98	7 (7.1)
Hamedi et al., 2020	Sheep	Different regions	Abomasal contents & Lung	150	36 (24.0)
Mosavi Yengejeh, 2021	Sheep	East Azerbaijan	Different tissues	48	4 (4.2)
Sharifi, 2021	Sheep	Khorasan Razavi	Liver	100	20 (20.0)
Heidari et al., 2018	Goat	Fars	Abomasal contents	117	18 (15.4)
Hamedi et al., 2020	Goat	Different regions	Abomasal contents & Lung	50	11 (22.0)

Table 6. Infection rate of *Coxiella burnetii* in aborted fetuses of ruminants from different regions of Iran based on polymerase chain reaction (PCR).

Reference	Group	Study area	Abortion fetal sample type	No. of sample	No. of positive (%)
Asadi, 2013	Sheep	Shiraz & Isfahan	Different tissues	67	0 (0.0)
Khalili et al., 2015	Sheep	Hamedan	Different tissues	30	0 (0.0)
Abiri et al., 2016	Sheep	Khorasan Razavi	Different tissues	92	16 (17.3)
Heidari et al., 2018	Sheep	Fars	Abomasal contents	183	5 (2.7)
Mahdavi Roshan et al., 2018	Sheep	Sistan va Bluchestan	Abomasal contents & spleen	78	13 (16.6)
Mahzounieh et al., 2019	Sheep	Different regions	Abomasal contents	98	0 (0.0)
Mohabati Mobarez et al., 2021	Sheep	Different regions	Different tissues	94	20 (21.8)
Heidari et al., 2018	Goat	Fars	Abomasal contents	117	1 (0.8)
Abiri et al., 2016	Cattle	Khorasan Razavi	Different tissues	60	PCR: 15 (25.0)
Mohabati Mobarez et al., 2021	Cattle	Different regions	Different tissues	46	PCR: 10 (21.7)

Table 7. Infection rate of *Toxoplasma gondii* in aborted fetuses of ruminants from different regions of Iran based on polymerase chain reaction (PCR).

Reference	Group	Study area	Aborted fetal sample type	No. of sample	No. of positive (%)
Rassouli, 2011	Sheep	Khorasan Razavi	Brain	200	27 (13.5)
Habibi et al., 2012	Sheep	Qazvin	Brain	18	12 (66.6)
Danehchin, 2014	Sheep	Khorasan Razavi	Brain	37	20 (54.0)
				112	18 (16.1)
Sanjarani, 2017	Sheep	Sistan va Baluchestan	Brain	79	13 (16.4)
Nourmohammadi, 2017	Sheep	Lorestan	Brain	142	10 (7.0)
		Khuzestan	Brain	127	10 (7.8)
Amouei et al., 2019	Sheep	Mazandaran	Brain	57	11 (19.3)
Shahbazi et al., 2019	Sheep	Ardabil	Brain	75	48 (64.0)
Salehi & Nezami, 2019	Sheep	North Khorasan	Different tissues	133	14 (10.5)
Partoandazanpoor et al., 2020	Sheep	Kurdistan	Brain	111	9 (8.1)
Malekifard et al., 2020	Sheep	West Azerbaijan	Brain & Placenta	130	7 (5.3)
Arefkhah et al., 2020	Sheep	Kohgiluyeh va Boyer-Ahmad	Brain	100	2 (2.0)
Nosrati et al., 2020	Sheep	Gilan	Brain	44	30 (68.2)
Azimi et al., 2021	Sheep	Mazandaran	Brain	48	8 (16.6)
Moravvej Hariri, 2021	Sheep	East Azerbaijan	Different tissues	30	0 (0.0)
Azimi et al., 2021	Cattle	Mazandaran	Brain	52	7 (13.4)
Partoandazanpoor et al., 2020	Goat	Kurdistan	Brain	10	1 (10.0)

Table 8. Infection rate of *Neospora caninumin* in aborted fetuses of ruminants from different regions of Iran based on polymerase chain reaction (PCR).

Reference	Group	Study area	Aborted fetal sample type	No. of sample	No. of positive (%)
Razmi et al., 2007	Cattle	Khorasan Razavi	Brain	100	13 (13.0)
Razmi et al., 2010	Cattle	Khorasan Razavi	Brain	151	18 (11.9)
Razmi et al., 2013	Cattle	Khorasan Razavi	Brain	200	23 (11.5)
Kamali et al., 2014	Cattle	Different regions	Brain	395	179 (45.0)
Rafati & Jaafarian, 2014	Cattle	Chahar Mahal va Bakhtiari	Brain	100	11 (11.0)
Kaveh et al., 2017	Cattle	Qazvin	Different tissues	128	39 (30.5)
Khani et al., 2018	Cattle	Markazi	Brain	38	10 (26.3)
Amouei et al., 2019)	Cattle	Mazandaran	Brain	9	2 (22.2)
Salehi et al., 2021	Cattle	Mazandaran	Brain	78	16 (20.5)
Asadpour et al., 2013	Sheep	Northwest regions	Different tissues	70	6 (8.5)
Sasani et al., 2013	Sheep	Different regions	Brain	109	1 (0.9)
Razmi & Naseri, 2017	Sheep	Khorasan Razavi	Brain	71	7 (9.8)
Amouei et al., 2019	Sheep	Mazandaran	Brain	57	2 (3.5)
Malekifard et al., 2020	Sheep	West Azerbaijan	Brain & Placenta	130	3 (2.3)
Salehi et al., 2021	Sheep	Mazandaran	Brain	51	8 (15.6)