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Review Article

Abortifacient Diseases in Bovine: A Comprehensive Review

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ABSTRACT

Livestock plays a vital role in the livelihoods of rural communities in developing countries including Pakistan, serving as a major source of income, nutrition, and social capital. The dependency on livestock has multifaceted implications for rural livelihoods and development. On one hand, it provides a source of income stability, particularly for smallholder farmers, landless laborers, and marginalized communities. Livestock also contributes to food security through the provision of milk, meat, and other animal products. There are several problems in the livestock industry one of them is abortifacient diseases that are responsible for pregnancy loss in bovine. Abortifacient diseases pose significant challenges to livestock production worldwide, resulting in substantial economic losses, decreased productivity, and threats to food security. This review provides an overview of the role of infectious diseases responsible for pregnancy loss in livestock specifically bovines, highlighting key pathogens, and modes of transmission. The impact of abortifacient diseases on cattle production extends beyond direct morbidity and mortality. These diseases disrupt reproductive performance, reduce fertility rates, decrease growth rates and impair feed conversion efficiency. In this review, common infectious diseases are described which are responsible for abortion in bovine, and their possible transmission, diagnosis and treatment are described.

INTRODUCTION

In Pakistan and other developing countries, livestock rearing and dairy production are the agricultural sector's principal economic activities. People living in rural areas are mostly dependent on agriculture and livestock. Improvements in reproduction can enhance the profitability of dairy producers. A high rate of pregnancy loss is one of the factors that decrease reproductive performance in some dairy herds [1]. One of the primary causes of decreased fertility is pregnancy loss (PL), which has a negative financial impact on dairy farmers [2, 3].

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Dairy cattle abortions increase the expense of reproduction, medical care, feeding, culling, and replacement rates [4]. Pregnancy loss in bovine has both infectious and non-infectious causes [5, 6]. Perhaps the most commonly assumed cause of abortions in humans and domestic animals is infectious agents [7]. Because these pathogenic organisms have the potential to cause significant financial losses, safety precautions and disease prevention are necessary [8]. Early diagnosis can help prevent and treat infectious diseases like trichomoniasis and vibriosis. To manage and avoid reproductive issues in their herd, dairy farmers should work with their veterinarians to establish a disease treatment and prevention program [9]. It is difficult to make a confirmatory diagnosis in bovine abortion, primarily when there are insufficient diagnostic tests available in the field [10]. Abortion results impair the ability of dairy cattle to reproduce. Furthermore, a longer postpartum period in cows that experience pregnancy loss may result in a higher culling rate [11].

This study aims to focus on the common bacterial, viral, protozoal and fungal diseases that cause bovine to have reproductive problems. Clinical signs are detailed, along with the diagnostic methods necessary for laboratories to accurately confirm the cause of abortion.

Abortion in Dairy Cattle

Abortion occurs when a pregnancy is ended between 45 and 260 days of gestation, at a point when the ejected fetus is recognizable in size and not viable [12]. Another definition of abortion provided by [13] is the delivery of a fetus before it reaches the stage of viability at which it can be seen with the unaided eye. Certain zoonotic diseases, like brucellosis and leptospirosis, can also induce abortion in cattle [4, 14]. Important infectious agents that have been linked to calf abortions include viruses, bacteria, protozoa, and several fungal species [15]. Furthermore, abortion can result from any illness that raises a fever [16]. Common Abortifacient Diseases in Bovines [17, 18] are shown (Table 1).

Table 1: Common Abortifacient Diseases in Bovine

Diseases	Occurrence of Abortion (Trimester)
Brucellosis	Third Trimester (Usually Around 7th Month)
Leptospirosis	Third Trimesters
Listeriosis	2nd or 3rd Trimesters
Compylobacteriosis	Between 4-7 Months
Trichomoniasis	1st Month to 4th Month
Bovine Viral Diarrhea (BVD)	1st or 2nd Trimesters
Infectious Bovine Rhinotracheitis (Ibr)	4th Month to End of Pregnancy
Neosporosis	2nd or 3rd Trimesters

Brucellosis

Brucellosis is a highly contagious zoonotic infection that affects both humans and animals and is an economically significant disease. It is the most prevalent zoonotic disease in the world [19]. Brucellosis may cause great loss of production through Abortion, stillbirth, orchitis, low herd fertility and decreased milk production [20]. In bovine, *Brucella abortus* causes brucellosis, which results in abortion, weak babies, fetal membrane retention, and low milk production. Usually, an abortion takes place during the seventh month of pregnancy. *Brucella abortus* is the main bovine pathogen [21]. Transmission of brucellosis primarily through fomites or direct contact with infected animals. Numerous pathogens are present in the fluid and fetal membranes of infected fetuses as well as in the vaginal discharges of recently aborted cows, making them a significant source of infection for other animals. Infected wild animals can also spread the disease to domestic livestock [22]. In cattle, brucellosis can also be spread by licking fetal membranes, aborted fetuses, or carrier cattle that have calved normally, as well as by consuming contaminated pasture, feed, and water. However, the mucosa at the conjunctiva and respiratory system often become infected when the skin is injured [23]. It is possible to prevent brucellosis by receiving the RB51 vaccine, in pregnant animals but live vaccines should be discouraged. The optimal time to vaccinate heifers is between 4 and 12 months of age. In certain high-risk circumstances, adult cattle may receive vaccinations. 131 The vaccination typically protects 70–80% of vaccinated animals, but it is not 100% effective. It is possible to implement vaccination and test-and-slaughtering policies on any age of population because Rifampicin-resistant and rough, *Brucella abortus* strain RB51 lacks the lipopolysaccharide o-side chain and does not generate antibodies against it that can be detected by standard serological testing [24].

Campylobacteriosis

Campylobacteriosis in bovine is caused by *Campylobacter fetus*. It can result in infertility, abortion, and early embryonic death in infected animals. Two significant animal pathogens that primarily affect the gastrointestinal and reproductive systems belong to the genus *Campylobacter* [25]. Abortion, embryonic mortality and poor reproductive performance are linked to bovine venereal campylobacteriosis. Cattle reproductive tracts and the internal organs of aborted fetuses have been found to harbour *Campylobacter fetus* subsp. *venerealis (Cfv)*, is the causative agent of this STD [25]. Bovine venereal campylobacteriosis is primarily spread by natural means, but it can also spread through artificial insemination (AI) when contaminated equipment or semen from infected bulls is used [26]. Direct transmission is unlikely between female cattle, the spread of infection but when animals are housed together during mounting behaviour, bull-to-bull can happen [27]. Endometritis and salpingitis are the

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results of the spread of bacteria to the womb and fallopian tubes in heifers as well as cows. After infection, pathology is most noticeable from 8 to 13 weeks later and usually goes away in 4 to 5 months. Though it usually results in a delayed return to oestrus and early embryonic death, infection does not affect conception. Although they can happen at any time, most abortions are discovered between four and six months of pregnancy. In female, the disease usually resolves on its own. The majority of cows recover and become pregnant in three to six months after infection, and immunity lasts for several years [28, 29]. Nevertheless, some cows may continue to harbour the infection for much longer [27]. In contrast, the infection in bulls does not cause lesions or the development of protective immunity. The preputial epithelium's crypts can become colonized by the bacteria, and the number and size of these crypts grow with bull age, allowing infection persistence [29, 28]. Investigating a possible case of bovine venereal campylobacteriosis begins with reviewing the reproductive history of the herd, performing a biosecurity audit, and determining whether or not there are any related clinical symptoms. Antigen detection in preputial washings is commonly accomplished by fluorescent antibody tests (FATs) [30]. After a Cfv abortion, secretory IgA (antigen-specific) antibodies can be found in the vaginal mucosa using enzyme-linked immunosorbent assay (ELISA). Although these antibodies have a long half-life, individual animals may experience false reactions due to antibody fluctuations [31]. Vaginal mucus agglutination tests (VMATs) are also frequently employed with a sensitivity of roughly 50%, to identify antibodies in vaginal mucus washings [26]. Bovine venereal campylobacteriosis can also be diagnosed using molecular techniques like sequence analysis and polymerase chain reaction (PCR) [32-34]. Evidence suggests that young bulls can recover spontaneously from bovine venereal campylobacteriosis. Bulls under three years old have reportedly responded well to both local and systemic antibiotic therapy; however, culling older bulls is typically advised. The most commonly used antibiotic is streptomycin, however, reports of C. fetus strains resistant to streptomycin have surfaced [35, 36]. It is not advised to treat infected cows and heifers because of the poor results and the majority of the females develop protective immunity that allows them to resist the disease [28, 29].

Leptospirosis

Leptospirosis is a major cause of meningitis, nephritis, septicemia, hepatitis, and abortion in cattle, especially in young animals. More than 260 antigenically different serovars from 25 serogroups, which are grouped into 9 pathogenic species, 5 intermediate, and 6 saprophytic species of *leptospira*, as well as a gram-negative bacterium from the Spirochaetales order, are the cause of leptospirosis [37]. The most common ways for transmission to happen are through contact with contaminated water, milk, post-abortion discharges, and the urine of infected animals. During pregnancy, cows may transfer bacterium to their womb transplacentally, and infected bulls may spread during coitus. Cattle with endemic reproductive issues due to *Leptospira serovars hardjo* and *pomona* experience abortions, premature births, fetal mummification, stillbirths, retained fetal membranes and the birth of weak calves. Furthermore, a more subdued syndrome marked by early embryonic death and subfertility has been linked to the disease [38]. Most abortions happen during the final trimester of gestation, but certain serovars can result in embryonic death, fetal mummification, or abortions in the second trimester. The abortion rate varies between 3 and 10% for L. hardjo and 50% for L. pomona. Histologically, certain cases show a slight inflammation of the fetal membranes, and certain silver stains may be able to detect the organism's presence. Renal tubular necrosis and interstitial nephritis occur in some fetuses [39]. The reverse transcription polymerase chain reaction (RT-PCR) is the best diagnostic technique to demonstrate leptospira DNA in the kidney of aborted fetuses. In vaccinated animals, serologic diagnosis of leptospirosis may prove difficult on a herd basis. Commonly used microscopic agglutination tests gauge. The quantity of antibodies in the mother's serum during the abortion and again two to three weeks later [40]. Laboratory techniques that are both direct and indirect are used to study animal leptospirosis. The detection is donr by methods that involve isolating the causative agent [41]. The diagnosis of leptospirae in urine or blood has been made directly by dark field microscopic inspection. However, leptospirae are frequently confused with artefacts, and the technique has poor sensitivity and specificity [42]. The identification of particular serum antibodies serves as the foundation for the indirect techniques of leptospirosis investigation. These techniques include the spot agglutination test, indirect immunofluorescence, and various ELISA tests that detect serum antibodies without serovar discrimination, or the microscopic agglutination test (MAT), which accurately detects the infecting serovars. The "gold standard" in serological testing is the microscopic agglutination test (MAT), despite its high labour costs and the need for maintaining multiple leptospiral serovars in the lab. Additionally, the test necessitates that the professional interpret the findings [43].

Bovine Viral Diarrhea

Bovine viral diarrhea (BVD) is a contagious disease caused by the Bovine Viral Diarrhea Virus (BVDV) that can lead to reproductive issues such as abortion, fetal malformations, and infertility in cattle. There is a significant economic threat from the BVDV to cattle worldwide. According to

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[44], it is a major factor in the reduced milk yield, reproductive issues, and diarrhea in affected herds. This virus is closely related to this *pestivirus*, which belongs to the *Flaviviridae family* [45]. The illness affects people and animals globally, with some animals experiencing subclinical infections [46]. Embryonic death may occur from fetal infection up to 45 days into pregnancy. Between 45 and 175 days of pregnancy, an abortion may happen after contracting cytopathic bovine viral diarrhea virus (cpBVDV). Pregnancy can cause a fetus to become persistently infected (PI) if non-cytopathic bovine viral diarrhea virus (ncpBVDV) infection happens before the fetus develops immune competence, which is typically between days 45 and 145. Most new acute and fetal infections originate from These PI animals that shed the virus through a range of bodily fluids, including semen, and typically do not develop BVDV antibodies. Premature death is the primary cause of mortality for most PI animals, with mucosal diseases resulting from ncpBVDV mutating into cpBVDV and superinfection occurring frequently. Numerous techniques have been developed to identify cattle infected with BVDV [45]. Among these are the isolation of viruses in the kidney, lung, testis, and other tissues of cows. Because serological tests, like ELISA, are utilized to ascertain the serostatus of a large number of animals sampled in a population, they are frequently utilized in exploratory studies [45].

Infectious Bovine Rhinotracheitis (IBR)

Infectious bovine rhinotracheitis (IBR) is caused by Bovine Herpesvirus 1 (BHV-1). Infection with IBR virus can lead to abortion and infertility in cattle. This infection is the primary cause of abortion among viral diseases in cattle is which has a 5–60% abortion rate in unvaccinated herds. Cattle populations are endemic to BHV-1, which causes several clinical syndromes such as conjunctivitis, respiratory disorders, encephalomyelitis, abortion, vulvovaginitis, balanoposthitis and fatal systemic infections in newborns [46]. All strain of BHV-1 has the potential to develop into a latent infection. A latently infected animal's semen or respiratory and reproductive secretions may contain virus particles due to stressful events such as calving, transportation, corticosteroid treatment, and other stressful situations. Following infection, BHV-1 in pregnant cows may remain latent in the placenta and only become active against the fetus after a few weeks. After becoming infected, the fetus dies rapidly and experiences autolysis before being expelled after remaining in the womb for several days. There is reddish-tinged edema in the subcutis. The pericardium, as well as the abdominal and thoracic cavities, contain large volumes of reddish-pink fluid [39]. The identification of BHV-1 can be achieved through several techniques such as real-time PCR, isolation of virus from fetal liver, lung and other tissues, EDTA-treated whole-blood samples, or adult animal semen [47].

Trichomoniasis

Trichomoniasis is caused by the protozoan *Tritrichomonas foetus.* It primarily affects the cattle's reproductive tract Trichomoniasis is a venereal disease that primarily affects pregnant animals. It can also occasionally cause abortion and pyometra, which can result in severe infertility. It is found worldwide and third most common cause of abortion in cattle, behind leptospirosis and brucellosis [48, 49]. When this organism is present, neither the bull nor the cow shows any symptoms of illness. Pyometra and early abortions (1-6 weeks) are also signs of the infection. Sometimes an infection prevents an abortion from occurring, and a healthy, full-term calf is born instead [50]. After an abortion, parasites typically vanish from vaginal discharges within seven days, and the aborted foetus is typically fresh [51]. For confirmatory diagnosis demonstration of *T. foetus* organisms from specimens taken from female cattle's genital tract, bull prepucial material or aborted foetal, and placental tissues confirms the diagnosis [52]. Additional diagnostic techniques comprise organism culture, PCR, and immunological testing [53, 54]. Trichomoniasis affects non-pregnant cows with involuted uteruses. Many cows experience an improvement in fertility and some level of immunity after three or five cycles of sexual rest. However, males who contract the infection become lifelong carriers of the pathogen; as a result, only clean bulls or semen should be used in breeding, and cows with deviant genital tracts should be put down [47]. "Carrier" bulls should be culled since they have the potential to infect susceptible, healed, and treated females again. As for the treatment of trichomoniasis in cattle, there isn't an approved chemotherapy drug [54].

Listeriosis

The infectious disease listeriosis is found all over the world and can affect both humans and animals. The three primary clinical signs are septicemia, meningoencephalitis, and abortion [55]. The majority of clinical cases have an infection with *Listeria monocytogenes. L. ivanovii* has only been linked to a small number of documented cases [16]. There are numerous species of Listeria in the environment. Silage that has not been properly preserved, fermented, or acidified enough to kill the bacteria can contain listeria. *Listeria monocytogenes* causes septicemia, encephalitis, and abortions in cattle. The late winter or early spring is when listeria infections and abortions typically occur. Abortions are most frequently detected in the final trimester of pregnancy [56]. Although ingestion is the primary route from where Listeria spp. enter the body, they can also get in through the respiratory system, or they can be injected into broken skin or eyes. *Listeria*

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monocytogenes nucleic acids and antigens have been detected in the placenta, fetus (such as the contents of the fetal stomach), or uterine discharges after an abortion; in the blood of animals suffering from sepsis; in samples taken from sites of localization, such as ocular swabs or cerebrospinal fluid (CSF); and in postmortem tissue samples, including the liver, kidneys, spleen, and brain. PCR can be used to detect nucleic acids in tissues and secretions. For *L. monocytogenes* and *L. ivanovii,* loop-mediated isothermal amplification (LAMP) assays have also been published. Antigens in tissues can be found using immunohistochemistry or immunofluorescence.

Neosporosis

Neosporosis is a protozoal disease caused by the *neospora caninum*. There are structural and genetic similarities between this parasitic protozoan and *Toxoplasma gondii.* The two species of *Neospora* that are currently known to exist are *Neospora caninum.* Cattle are among the intermediate hosts of *N. caninum,* with dogs serving as the definitive host [57, 58]. Oocysts excreted in dog feces can contaminate feed and water, or cattle can contract the infection congenitally [59, 60]. According to reports from populations of beef and dairy cattle worldwide, this parasite is the main cause of abortion and neonatal mortality [61, 62]. *Neospora caninum* can cause abortions in cattle as early as three months of gestation, although they happen most frequently between five and six months. It has been reported that abortion storms in cows or endemic abortions are connected to *neospora.* An important factor in the epidemiology of neosporosis is congenital/vertical transmission from seropositive dams to their offspring, and the incidence of abortion is frequently repeated in subsequent gestations [63, 64]. These include the histopathology of tissues from stillbirths and aborted fetuses, the extraction of parasites from sacrificed animals, the inoculation of mice, the use of molecular techniques like PCR, and the recovery of oocysts from dog feces. Nonetheless, because serology can be performed both antemortem and postmortem, it is the most widely used method for diagnosing neosporosis (ELISA and immune-fluorescent antibody test). Since serology is utilized to accurately test exposure and infection in populations of numerous animals, it is helpful in epidemiological studies [63].

DIAGNOSTIC METHODS OF BOVINE ABORTION

When diagnosing abortion in dairy animals, general guidelines include gathering all epidemiological information, including recent introductions into the farm, counting the impacted animals, closely inspecting the affected dam or dams, and gathering the ejected fetus and placenta for microbiological and pathological analysis. A diagnosis is then made by compiling and analyzing the data [16]. However, due to the wide variety of pathogens involved and the possibility of factors affecting the dam, fetus, and placenta, the diagnostic rate for bovine abortions is extremely low [61, 65]. Additionally, an abortion frequently happens after an initial infection that may have persisted for a few weeks or months; by the time the abortion takes place, the etiology is frequently undetectable. The issue is further exacerbated by the high expense of laboratory testing required to help diagnose bovine abortion [66]. An organized herd's records are frequently helpful when looking into abortion-related issues [67]. It is necessary to remember that there are many different reasons why cattle abort, making diagnosis difficult in many cases [67]. To improve the interpretation of laboratory results, the field of investigation could be narrowed down with the use of epidemiological tools [17].

CONCLUSIONS

Abortion is one of the necessary reproductive health issues faced by dairy cows when it comes to the financial effects. In cattle, abortion can be caused by infectious or non-infectious agents. Hereditary and non-genetic disorders are examples of non-infectious variables. Stress-related to heat, production, changing seasons, and seasonal effects is the non-genetic causes of abortion, neosporosis, leptospirosis, listeriosis, brucellosis, and bovine viral diarrhea are among the common infectious causes of abortion in cattle. These infectious diseases not only result in direct economic losses due to abortion and reduced productivity but also pose public health risks. Control measures are necessary to prevent abortion because these causes can lead to significant economic losses. The main focus of attention of this review is on the infectious causes of abortion. The causes of abortion should be investigated, and controls should be put in place.

Authors Contribution

Conceptualization: SAL, AS, FURS, FH, TM,
Methodology: SAL
Formal analysis: QK, MMR
Writing review and editing: SAL, AS, FURS, FH, TM, IU, AR

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

All the authors declare no conflict of interest.

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