ISSN 2664-4169 (Print) & ISSN 2664-7923 (Online)
South Asian Research Journal of Biology and Applied Biosciences
Abbreviated Key Title: South Asian Res J Bio Appl Biosci

| Volume-8 | Issue-5 | Sep-Oct -2026 | **DOI: https://doi.org/10.36346/sarjbab.2026.v08i05.003**

Review Article

Bovine Respiratory Disease Complex: Pathogenesis, Diagnostic Tools, and Novel Therapeutic Approaches

Aomnea M. Abdulazeez[1]*, Raghad Alnuaimy[2]

[1]Anesthesia Techniques Department, Mosul Medical Technical Institute, Northern Technical University
[2]Department of Animal Production, College of Agriculture & Forestry, University of Mosul, Iraq

***Corresponding Author:** Aomnea M. Abdulazeez
Anesthesia Techniques Department, Mosul Medical Technical Institute, Northern Technical University

Article History
Received: 29.06.2026
Accepted: 22.08.2026
Published: 28.09.2026

Abstract: Bovine respiratory disease complex (BRDC) is one of the most important multifactorial disease syndromes affecting cattle and is associated with substantial economic losses through morbidity, mortality, treatment costs, and reduced production efficiency. BRDC develops through complex interactions among environmental and management stressors, host factors, primary viral infections, and secondary bacterial pathogens. This review summarizes current knowledge of BRDC pathogenesis, diagnostic approaches, and therapeutic and preventive strategies. Important viral agents include bovine respiratory syncytial virus, bovine parainfluenza virus type 3, bovine herpesvirus-1, and bovine viral diarrhea virus, while major bacterial pathogens include Mannheimia haemolytica, Pasteurella multocida, Histophilus somni, and Mycoplasma bovis. Viral infection and stress can impair respiratory defenses and facilitate bacterial colonization of the lower respiratory tract. Diagnosis remains challenging because clinical signs are often nonspecific and molecular detection may identify organisms that are present without being the primary cause of disease. Multiplex quantitative PCR has expanded the capacity for simultaneous pathogen detection, but results must be interpreted together with clinical, pathological, and epidemiological findings. Effective control requires integrated herd management, including stress reduction, biosecurity, strategic vaccination, early diagnosis, and prudent antimicrobial use. Future advances will depend on improved vaccines, better host-response biomarkers, refined diagnostics, and sustainable alternatives to conventional antimicrobial therapy.

Keywords: Bovine Respiratory Disease Complex, BRDC, Cattle, Viral-Bacterial Synergy, Molecular Diagnostics, Vaccination; Antimicrobial Stewardship.

1. INTRODUCTION

Bovine respiratory disease (BRD), commonly referred to as bovine respiratory disease complex (BRDC), is a multifactorial respiratory syndrome of major importance in cattle production. The disease results from interactions among environmental stressors, host susceptibility, and multiple infectious agents. BRDC is particularly important in recently weaned, transported, and commingled cattle, where stress and pathogen exposure can occur simultaneously [8].

Unlike a disease caused by a single organism, BRDC involves a complex sequence of events. Stressors such as weaning, transportation, crowding, commingling, inadequate ventilation, and adverse weather can weaken host defense mechanisms and increase exposure to infectious agents. Primary viral infection can further compromise respiratory defenses and facilitate colonization of the lower respiratory tract by opportunistic bacteria [8].

The major pathogens associated with BRDC include bovine herpesvirus-1 (BHV-1), bovine respiratory syncytial virus (BRSV), parainfluenza-3 virus (PI-3), and bovine viral diarrhea virus (BVDV), together with Mannheimia haemolytica, Pasteurella multocida, Histophilus somni, and Mycoplasma bovis [1-8]. This review discusses the pathogenesis of BRDC, diagnostic developments, and current therapeutic and preventive approaches.

2. PATHOGENESIS: THE VIRAL-BACTERIAL SYNERGY

BRDC develops through the interaction of predisposing stressors and infectious agents. Stress and viral infection can suppress immune defenses and alter the respiratory environment, allowing bacteria that normally inhabit the upper respiratory tract to proliferate and colonize the lower respiratory tract [1-8].

2.1. Predisposing Factors and Viral Pathogens

Transportation, weaning, commingling, crowding, poor ventilation, nutritional stress, and adverse weather are important risk factors for BRDC. These factors can impair specific and nonspecific host defense mechanisms while also increasing transmission opportunities among cattle [8].

BHV-1, BRSV, PI-3, and BVDV are among the most important viral pathogens associated with BRDC. Viral infections can damage respiratory tissues, interfere with mucociliary clearance, and alter immune responses. BRSV is especially important because of its ability to affect the lower respiratory tract and predispose cattle to secondary bacterial infection [6].

The interaction between viral and bacterial pathogens is central to BRDC pathogenesis. Viral infection may increase susceptibility to bacterial colonization, while bacterial toxins and inflammatory responses contribute to severe pulmonary injury [1].

2.2. Major Bacterial Pathogens

2.2.1. Mannheimia Haemolytica

Mannheimia haemolytica is a major bacterial cause of BRDC and is frequently associated with severe acute fibrinous pneumonia. After stress or viral infection, the organism can proliferate in the upper respiratory tract and subsequently colonize the lungs. Leukotoxin is an important virulence factor that contributes to leukocyte damage, inflammation, and pulmonary tissue injury [3-6].

2.2.2. Pasteurella Multocida

Pasteurella multocida is an opportunistic pathogen associated with acute and chronic forms of bovine pneumonia. It often occurs in polymicrobial infections and possesses virulence factors that support colonization and persistence, including capsular and surface-associated components [3].

2.2.3. Histophilus Somni

Histophilus somni is another important bacterial agent associated with BRDC. In addition to pneumonia, infection can be associated with systemic disease, including myocarditis and thrombotic meningoencephalitis. Disease development is influenced by host immunity and concurrent respiratory infections [6].

2.2.4. Mycoplasma Bovis

Mycoplasma bovis has a distinctive role because it lacks a cell wall and can persist through antigenic variation and other immune-evasion mechanisms. It is associated with chronic respiratory disease and presents diagnostic challenges because detection may reflect colonization as well as active disease [1-5].

2.3. Host Immune Evasion and Immunosuppression

BRDC pathogens employ multiple mechanisms that reduce the effectiveness of host defenses. Viral infections can compromise mucosal barriers and immune-cell function, whereas bacterial pathogens can produce toxins and other virulence factors that interfere with immune clearance. The combined effects of stress, viral infection, and bacterial invasion help explain the severity and variability of BRDC [1].

3. DIAGNOSTIC TOOLS: FROM CLINICAL SCORING TO MOLECULAR DETECTION

Accurate diagnosis is essential for effective BRDC management, but it remains difficult because clinical signs are often nonspecific and multiple pathogens can be detected simultaneously. Consequently, diagnosis should integrate clinical examination, herd history, laboratory testing, and pathological findings when available [2].

3.1. Clinical Assessment and Scoring Systems

Clinical assessment commonly includes evaluation of depression, appetite, coughing, nasal discharge, respiratory effort, lung sounds, and rectal temperature. Clinical scoring is useful for identifying affected animals but may have limited sensitivity and specificity. A consistent clinical definition can improve disease recognition and treatment decisions [2].

3.2. Molecular Diagnostics

PCR and quantitative PCR have improved the detection of BRDC-associated pathogens. Multiplex assays can simultaneously detect several viral and bacterial agents, supporting investigation of mixed infections. Li *et al*., [4], reported

a multiplex real-time qPCR assay targeting six important BRDC-associated pathogens, illustrating the growing role of molecular diagnostics in rapid pathogen detection.

However, molecular detection must be interpreted carefully. The identification of a pathogen does not always demonstrate that it is the primary cause of clinical disease, particularly when organisms may be carried by apparently healthy cattle. Sample type, timing of collection, clinical status, and pathogen burden should therefore be considered during interpretation [1-6].

3.3. Diagnostic Challenges for Mycoplasmas

Mycoplasma bovis detection is particularly challenging because respiratory carriage can occur without clear evidence of causation. Diagnostic interpretation should therefore combine molecular results with clinical findings, lesion patterns, and herd epidemiology [5].

3.4. Emerging Biomarkers and Prognostic Indicators

Research into host-derived biomarkers may provide additional tools for early disease detection and prognosis. Biomarkers of inflammation and tissue injury could complement pathogen detection, although further validation is needed before many candidates can be routinely applied in field conditions [1].

4. THERAPEUTIC AND PREVENTIVE APPROACHES

Because BRDC is multifactorial, successful control requires integrated strategies rather than reliance on a single intervention. Stress reduction, vaccination, biosecurity, accurate diagnosis, and responsible antimicrobial use should be coordinated within herd-specific health programs [8].

4.1. Vaccination

Vaccination is an important component of BRDC prevention, but effectiveness can vary according to vaccine type, timing, animal age, maternal antibodies, pathogen exposure, and management conditions. Vaccination strategies should therefore be adapted to herd-specific risks and implemented as part of a broader preventive program [9].

Yarnall *et al*., [9], identified practical barriers to BRDC vaccination, including limited awareness of disease impact, uncertainty regarding optimal timing, concerns about vaccine efficacy, and resistance to changing established management practices. Diagnostic testing and farm-specific health assessments can help improve vaccination decisions.

4.2. Antimicrobial Therapy and Stewardship

Antimicrobial therapy remains important for bacterial BRDC when clinically indicated. Early identification and treatment of appropriate cases can improve animal welfare and outcomes. Nevertheless, unnecessary antimicrobial use can contribute to antimicrobial resistance, making diagnostic support and stewardship increasingly important [8].

4.3. Biotherapeutics and Alternative Strategies

Alternative strategies, including probiotic approaches, immunostimulants, and improved vaccine formulations, are being investigated to reduce dependence on conventional antimicrobials. These approaches are promising but require further controlled studies to establish consistent field effectiveness [1].

4.4. Integrated Herd Management

Integrated management is central to BRDC prevention. Important measures include minimizing transport stress, reducing unnecessary commingling, maintaining adequate ventilation, providing appropriate nutrition and water, applying biosecurity measures, and using strategic vaccination. Preconditioning can reduce risk by separating stressful procedures and allowing cattle time to adapt before transport and feedlot entry [8].

5. CONCLUSION AND FUTURE DIRECTIONS

BRDC remains a major challenge to cattle production because of the complex interactions among host factors, environmental stress, viral pathogens, and bacterial agents. Advances in molecular diagnostics have improved pathogen detection, but accurate interpretation still requires integration with clinical and epidemiological evidence. The most effective control programs combine stress reduction, biosecurity, vaccination, early diagnosis, and prudent antimicrobial use.

Future research should focus on improving vaccine effectiveness, identifying reliable host-response biomarkers, distinguishing colonization from active infection, understanding polymicrobial interactions, and developing sustainable alternatives to conventional antimicrobial therapy. A stronger integration of molecular diagnostics with herd-level epidemiology will be essential for improving BRDC prevention and control.

REFERENCES

1. Bell RL, Turkington HL, Cosby SL. The bacterial and viral agents of BRDC: Immune evasion and vaccine developments. Vaccines. 2021;9(4):337. doi:10.3390/vaccines9040337.
2. Buczinski S, et al. Scoping review on clinical definition of bovine respiratory disease complex and related clinical signs in dairy cows. Journal of Dairy Science. 2021;104(6):7095–7108. doi:10.3168/jds.2020-19471.
3. Griffin D, Chengappa MM, Kuszak J, McVey DS. Bacterial pathogens of the bovine respiratory disease complex. Veterinary Clinics of North America: Food Animal Practice. 2010;26(2):381–394.
4. Li L, Jiang Q, Li S, et al. Establishment of a multiplex qPCR assay for the detection of pathogens associated with bovine respiratory disease complex. Frontiers in Veterinary Science. 2025;12:1594488. doi:10.3389/fvets.2025.1594488.
5. Maunsell FP, Woolums AR, Francoz D, et al. Mycoplasma bovis infections in cattle. Journal of Veterinary Internal Medicine. 2011;25:772–783.
6. Renaud D, Abuelo A. Viral infections associated with bovine respiratory disease complex in cattle. Merck Veterinary Manual. 2024.
7. Renaud D, Abuelo A. Bacterial pneumonia in cattle with bovine respiratory disease complex. Merck Veterinary Manual. 2024.
8. Renaud D, Abuelo A. Overview of bovine respiratory disease complex. Merck Veterinary Manual. 2025.
9. Yarnall M, Amovilli F, Assié S, Bokma J, Pugh M, Werling D. Identifying and addressing barriers and opportunities for bovine respiratory disease complex vaccination: A consensus paper on practical recommendations for best practise vaccination. Frontiers in Veterinary Science. 2024;11:1368060. doi:10.3389/fvets.2024.1368060.