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Mastitis: Pathogenesis, Causative Agents, and Future Perspectives

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ABSTRACT

The inflammation of the mammary gland, which is known as mastitis, continues to be among the most important and financially crippling diseases in the world in relation to dairy animals. The condition will result in low milk production, altered milk composition, and permanent damage to the udder, leading to severe economic losses for dairy farmers. It is a multifactorial disease that entails the complex interplay between pathogens, host defense mechanisms, and environmental factors. The current review is devoted to the pathogenesis, etiological factors, and prevention of bovine mastitis in detail, with reference to the difficulties and perspectives, as well as prospects in Pakistan. Pathogenesis entails the entry of bacteria via the teat canal, activation of the innate and adaptive immune system, and discharge of the inflammatory mediators, resulting in tissue damage. Some of the significant pathogenic bacteria are *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus agalactiae*, and *Mycoplasma bovis*. The increasing issue of antimicrobial resistance and the sustainable strategies of its control are also considered in the review, as well as new methods, including vaccination, phytotherapy, and nanotechnology-based drug delivery systems. To establish sustainable local production of dairy in Pakistan and other parts of the world, it is imperative to understand molecular processes and local epidemiology better, with an aim of introducing targeted and cost-effective mastitis control measures.

Keywords: Dairy Cattle, Pakistan, Udder Health, Antimicrobial Resistance, Pathogenesis, Mastitis

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Introduction

Mastitis can be defined as inflammation of the parenchyma of the mammary gland, which is a physical, chemical, and microbiological change in milk and pathological changes in glandular tissue [1]. It is considered to be one of the most widespread and expensive diseases in dairy cattle, which influences the quantity and quality of milk. Mastitis contributes to the dairy industry by causing as many as 40% of economic losses globally in the dairy industry, compared to the reproductive and metabolic diseases. Economic losses are done by the way of reduced milk production, wasted milk, treating the milk, and untimely culling. In the United States and Europe, yearly economic damages attributed to mastitis are over USD 2 billion, and in South Asia, the amount is hard to estimate, as there is underreporting and illegal milk markets [2]. In Pakistan, the dairy industry is currently giving over 11 percent contribution to the national GDP, although mastitis is rampant, with prevalence rates of between 25 percent and 60 percent in bovines. The most widespread and economically insidious type is subclinical mastitis, which manifests itself in high somatic cell count but no visible signs. In Pakistan, the following are considered to be risk factors: unhygienic milking, contaminated housing, unsanitary udders, and farmer ignorance. Disease is further increased by seasonal variations, heat stress, and inappropriate milking of the machine [3].

Mastitis may be of types

Clinical mastitis: Observable inflammation, unnatural milk, and systemic disease.

Subclinical Mastitis: There are no visible symptoms, and there is an elevated level of somatic cell count (SCC).

Chronic Mastitis: Recurrent infections with irreparable tissue damage to the udder.

The knowledge of how infections, immune response, and pathogen survival strategies work is the key to creating preventative and therapeutic strategies based on local conditions [4].

Pathogenesis of Mastitis:

The pathogenesis of mastitis is a complex mechanism that includes invasion of microbes, activation of host immunity, and inflammatory destruction. Most of the time, the infection starts with the introduction of the pathogenic microorganisms into the udder by the teat canal and settling in the mammary epithelium.

- **Invasion and Colonization of Pathogens:**

The teat canal provides the initial defense against the pathogens. The sphincter becomes open during milking or injury of the teats, permitting the entry of bacteria into the external environment. *S. aureus* and *E. coli* pathogens attach themselves by use of adhesins, fimbriae, and biofilm-forming proteins to the epithelial cells [5]. The formation of biofilms improves the resistance of bacteria to antibiotics and immune clearance, which adds to chronic and recurrent infections.

- **Host Immune Recognition and Activation:**

After bacteria invade the epithelial barrier, microbial constituents, especially lipoteichoic acid (LTA) in Gram-positive and lipopolysaccharide (LPS) in Gram-negative bacteria, are recognized by innate immune receptors, especially Toll-like receptors. TLR activation causes the release of pro-inflammatory cytokines (NF-kB) signaling pathway (TNF-α, IL-1, IL-6, and IL-8) into the bloodstream [6]. Such cytokines attract neutrophils and macrophages to the place of infection. Neutrophils ingest bacteria and empty reactive oxygen species (ROS) and proteolytic enzymes in order to eliminate pathogens. Nonetheless, overproduction of inflammatory reactions is also harmful to mammary epithelial cells, leading to tissue necrosis, edema, and a reduction in milk secretion.

- **Cellular and Molecular Damage:**

Recent research indicates that oxidative stress contributes significantly to tissue damage in the condition of mastitis. An increase in ROS leads to lipid peroxidation, mitochondrial dysfunction, and mammary cell apoptosis [7]. It causes the loss of milk proteins, a higher number of somatic cells, and low-quality milk. Caspase-3 and Bax are apoptotic markers that are highly increased in mastitis.

- **Resolution or Chronicity:**

When the bacterial eradication is successful, anti-inflammatory cytokines like IL-10, as well as TGF-β, are used to restore tissue homeostasis. Nevertheless, certain pathogens, in particular, *S. aureus*, escape clearance by immune cells by inhabiting a host cell or developing micro-abscesses [8]. The result is chronic infections that are unresponsive to treatment and develop into chronic mastitis.

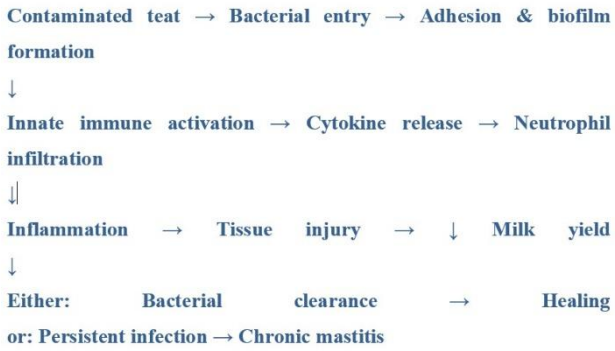

Fig. 1: Simplified Pathogenesis of Mastitis

Causative Agents of Mastitis

There is a great number of pathogens that cause mastitis, such as bacteria, mycoplasmas, fungi, and viruses [9]. These may be classified into environmental and contagious pathogens.

Contagious Pathogens

These are the pathogenic organisms that are mostly passed through contaminated equipment, hands, or towels during the milking process.

- *Staphylococcus aureus*: This is a primary cause of contagious mastitis. It produces coagulase, leukotoxins, and proteases, which help it to destroy tissues and cause abscesses [10]. It develops biofilms, which increase persistence.
- *Streptococcus agalactiae*: This is an obligate udder pathogen (very contagious) and sensitive to penicillin.
- *Mycoplasma bovis*: Causes severe mastitis, arthritis, and pneumonia, non-responsive to traditional antibiotics because of an absence of a cell wall.
- *Corynebacterium bovis*: A Small pathogen, which is located in the teat canals, is a sign of low hygiene.

Environmental Pathogens:

The bacteria are acquired through the bedding, manure, soil, or impure water.

- *Escherichia coli*: This produces endotoxins that result in acute clinical mastitis with systemic symptoms.
- *Klebsiella spp*: Dust-bedded and often associated with sawdust, and characterized by extreme antibiotic resistance.
- *Streptococcus uberis*: This is prevalent in herds that are kept in pastures and produces persistent subclinical infection [11].

Fungal and Viral Agents:

Mostly due to the prolonged use of antibiotic therapy, fungal mastitis is a secondary disease caused by *Candida albicans*, *Aspergillus*, and *Trichosporon* species [12]. Secondary bacterial invasion of the udder can be predisposed by the viral infections, including the bovine herpesvirus 1 (BoHV-1) and parainfluenza virus.

Emerging Pathogens

Recent reports show that *coagulase-negative staphylococci* (CNS) species, including *S. chromogenes* and *S. epidermidis,* have been on the increase and are opportunistic but not insignificant in subclinical cases. The topic of antimicrobial resistance of mastitis pathogens will be discussed. The rapid emergence of antimicrobial resistance (AMR) has resulted from the indiscriminate use of antibiotics in dairy farms [2]. In Pakistan, extended-spectrum beta-lactamase (ESBL)- producing E. coli and methicillin-resistant Staphylococcus aureus (MRSA) are becoming increasingly common. β-lactamase production, efflux pumps, and protection through biofilm are the mechanisms of resistance [13]. AMR not only complicates treatment but also represents a health hazard to people because it contains residues of antibiotics in milk. The key steps that should be taken to reduce AMR are strengthening antimicrobial stewardship, periodic sensitivity tests, and educating farmers, therapists, and management plans.

Antibiotic Therapy:

Antibiotics still form the primary therapy in the management of mastitis, but a culture and sensitivity test must inform their use.

Antibiotic Class	Examples	Target Pathogens	Reference
Beta-lactams	Penicillin, Cloxacillin	*S. aureus*, *Strep. agalactiae*	[14]
Cephalosporins	Ceftiofur, Cefalexin	*E. coli*, *Klebsiella spp.*	[15]
Macrolides	Erythromycin, Tylosin	*Mycoplasma bovis*	[16]
Aminoglycosides	Gentamicin, Neomycin	*Pseudomonas spp.*	[17]

Excessive and inappropriate use of these drugs causes AMR and milk residues, which may be harmful to consumers. Supportive therapy, anti-inflammatory medications, improving healing, fluid therapy, and udder massage, improves healing.

Preventive Measures

The most recent mastitis control program that meets the gold standard is the five-point program: Post-milking teat dipping. Dry cow antibiotic therapy. Effective maintenance of the milking machine. Early intervention in patient cases. The elimination of long-term infected cows. In Pakistan, this is usually sabotaged by a lack of training of farmers and poor milking hygiene [18]a. Community-level milk hygiene programs and veterinary extension services implementation are required.

Future Perspectives

Vaccination against S. aureus and E. coli has partially worked. The combination of surface antigens, toxoids, and those associated with biofilms can be effective. Pakistan could also get better results by using locally isolated strains to produce vaccines against dairy herds. *Lactobacillus* and *Bifidobacterium* can colonize the udder and prevent the growth of pathogen by excluding them through competition and producing *bacteriocin*. Vitamin E, selenium, and herbal extracts (neem, turmeric, aloe vera) are immune-modulators, which increase resistance to infection and can be included in preventive measures. The nanoparticles have strong antibacterial activity particularly silver, zinc oxide and chitosan which can be used to deliver drugs to infected tissues in a specific manner. They lower the amount of dose and decrease the levels of antibiotics in milk. Omics technologies also lead to the discovery of genes that are associated with mastitis resistance, which can be used to selectively breed animals using markers. Proteomic analysis of milk can be used to report biomarker early mastitis to enhance monitoring of health of farm animals. Subclinical mastitis can be identified with the help of automated sensors, milk conductivity meter, and thermal imaging. These tools combined with artificial intelligence and machine learning may transform the management of mastitis in the future.

Conclusion

Mastitis remains a significant challenge to the dairy profitability, the animal health, and the society especially in developing economies such as Pakistan. This multidisciplinary approach necessitates an improved farm hygiene, prudent use of antibiotics, and innovative technologies as the multifactorial nature of it demands. An effective prevention and control will be made possible through a detailed knowledge of the immune-pathogenesis, the virulence of the pathogen, and the host genetics. Combination of conventional interventions with new strategies like vaccination, probiotics, nanotechnology, and genomic selection is promising to maintain mastitis and control it as well as enhance the health of the udder of the dairy cattle in the world.

References

[1] Qureshi MA, Fatima Z, Muqadas SM, Najaf DE, Husnain M, Moeed HA, Ijaz U. Zoonotic diseases caused by mastitic milk. Zoonosis, Unique Scientific Publishers, Faisalabad, Pakistan. 2023; 4:557-72.

[2] Paramasivam, R., et al., Is AMR in dairy products a threat to human health? An updated review on the origin, prevention, treatment, and economic impacts of subclinical mastitis. Infection and Drug Resistance, 2023: p. 155-178.

[3] Ame, M.M. and S. Mengistu, ISOLATION AND IDENTIFICATION OF Escherichia coli FROM RAW COW MILK AND THE POSSIBLE SOURCE OF CONTAMINATION IN DAIRY FARMS FOUND IN AND AROUND HARAMAYA EASTERN HARERGHE, ETHIOPIA. 2023.

[4] Lionakis, M.S., R.A. Drummond, and T.M. Hohl, Immune responses to human fungal pathogens and therapeutic prospects. Nature Reviews Immunology, 2023. 23(7): p. 433-452.

[5] Bhattacharya, M. and A.R. Horswill, The role of human extracellular matrix proteins in defining Staphylococcus aureus biofilm infections. FEMS Microbiology Reviews, 2024. 48(1): p. fuae002.

[6] Manik, M. and R.K. Singh, Role of toll-like receptors in modulation of cytokine storm signaling in SARS-CoV-2-induced COVID-19. Journal of medical virology, 2022. 94(3): p. 869-877.

[7] Lee, W., et al., Diflubenzuron leads to apoptotic cell death through ROS generation and mitochondrial dysfunction in bovine mammary epithelial cells. Pesticide biochemistry and physiology, 2021. 177: p. 104893.

[8] Pidwill, G.R., et al., The role of macrophages in Staphylococcus aureus infection. Frontiers in immunology, 2021. 11: p. 620339.

[9] Gelgie, A.E., M.G. Korsa, and O.K. Dego, Mycoplasma bovis mastitis. Current Research in Microbial Sciences, 2022. 3: p. 100123.

[10] Fayisa, W.O. and N.F. Tuli, Review on Staphylococcus aureus. Int. J. Nurs. Care Res, 2023. 1: p. 1-8.

[11] van Lelyveld, G.K., Molecular characterization of Streptococcus uberis strains, isolated in a longitudinal study from milk of a commercial South African dairy herd. 2025.

[12] Pal, M., Etiology, transmission, epidemiology, clinical spectrum, diagnosis and management of fungal mastitis in dairy animals: A mini review. International Journal of Food Science and Agriculture, 2023. 7(3): p. 424-429.

[13] Lorusso, A.B., et al., Role of efflux pumps on antimicrobial resistance in Pseudomonas aeruginosa. International journal of molecular sciences, 2022. 23(24): p. 15779.

[14] Vilvanathan, S., Penicillins, Cephalosporins, and Other β-Lactam Antibiotics, in Introduction to Basics of Pharmacology and Toxicology: Volume 2: Essentials of Systemic Pharmacology: From Principles to Practice. 2021, Springer. p. 821-834.

[15] Nayeem, A., et al., Comprehensive Insights into Cephalosporins: Spectrum, Generations, and Clinical Applications. Current Drug Therapy, 2024.

[16] Prescott, J.F. and K.E. Baptiste, Macrolides, Azalides, and Ketolides. Antimicrobial Therapy in Veterinary Medicine, 2024: p. 223-248.

[17] Qureshi, N.K. and M.H. Rathore, Aminoglycosides. 2025, American Academy of Pediatrics Itasca, IL, USA.

[18] Nadeem, M. and M.H. Ahmad, Sustaining the dairy sector in Pakistan: challenges and strategies for growth. 2024.