

Abstract

# Microbial Underpinnings of Mastitis: Current State of the Evidence <sup>†</sup>

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**Abstract:** Mastitis is an inflammatory condition of the breast, with or without accompanying infection. The recent release of the revised Academy of Breastfeeding Medicine protocol on mastitis (Clinical Protocol #36) has caused controversy within the field. The updated protocol positions multiple typical human milk commensal bacteria as causative agents of mastitis. However, data to support these relationships are lacking. Here, we critically review human and animal evidence for the role of the milk microbiota in mastitis. Only three metataxonomic/metagenomic studies have characterized the human milk microbiome in cases of mastitis. These studies consistently report reduced alpha diversity and elevated levels of *Staphylococcus aureus* in mastitic milk samples; however, the remaining findings presented are conflicting and inconsistent. Collectively, the three studies included 45 sub-acute mastitis cases, 24 acute mastitis cases, and 52 healthy controls, and are thus limited by low participant numbers. In addition, the studies vary in their definition of sub-acute/acute mastitis, their methodologies, and antibiotic exposure in the mastitic groups. Further, these studies provide data on the state of the microbiome during mastitis, with no data currently available on the milk microbiome preceding the onset of mastitis. These kind of longitudinal data are critical to identify candidates for disease causation. Emerging evidence from animal models is suggestive of the involvement of the gut microbiota. Studies have reported that fecal microbiota transplantation from mastitic cows to germ-free mice results in mastitis symptoms. Future studies should therefore consider the maternal microbiome more broadly when assessing the etiology of mastitis. While *S. aureus* is frequently recognized as a mastitis-related pathogen, data from culture-based and culture-independent studies demonstrate that this species is present in healthy women and cannot be detected in a significant portion of cases. This suggests heterogenous causes for bacterial mastitis, necessitating broader screening. Overall, data in this field are sparse, and current clinical guidelines lack high-quality evidence to support them. There is therefore a pressing need for further research in this area to better characterize the causes of mastitis and thereby underpin future therapeutics.



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