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ONE HEALTH APPROACH TO ANTIMICROBIAL RESISTANCE IN MASTITIS: EXPLORING SUSTAINABLE TREATMENT ALTERNATIVES

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RESUMO: A resistência antimicrobiana (RAM) na mastite bovina tornou-se uma preocupação crescente para a saúde pública e veterinária, comprometendo a eficácia dos tratamentos convencionais e elevando os custos de manejo. A mastite é causada principalmente por *Staphylococcus aureus* e *Escherichia coli*, patógenos que têm demonstrado resistência crescente a antibióticos comuns, como penicilina e tetraciclina. A abordagem One Health, que integra os setores da saúde humana, animal e ambiental, surge como uma estratégia eficaz para combater a resistência e melhorar a eficácia dos tratamentos. Este estudo revisou sistematicamente artigos publicados entre 2020 e 2025, utilizando as bases de dados PubMed, BIREME e SciELO, com o objetivo de avaliar como a abordagem One Health impacta a RAM na mastite e explorar alternativas terapêuticas sustentáveis. Foram selecionados 19 artigos que atendiam aos critérios de inclusão, abordando a prevalência da RAM nos patógenos causadores da mastite, bem como o uso de vacinas e fitoterápicos como alternativas ao uso de antibióticos. Os resultados mostraram que a resistência aumentou principalmente devido ao uso excessivo de antibióticos, enquanto a abordagem One Health demonstrou ser promissora no controle da resistência ao integrar práticas da saúde veterinária, saúde pública e meio ambiente. Além disso, alternativas sustentáveis, como vacinas e fitoterápicos, mostraram-se eficazes na redução da resistência, sem introduzir novos problemas relacionados à resistência. Conclui-se que a implementação da abordagem One Health, combinada com alternativas sustentáveis, oferece um modelo eficaz para o controle da resistência antimicrobiana na mastite bovina. No entanto, é importante destacar a escassez de estudos aprofundados sobre a eficácia e viabilidade dessas alternativas terapêuticas a longo prazo. A ausência de dados robustos limita a aplicação dessas soluções no campo e reforça a necessidade urgente de novos estudos que confirmem sua eficácia em larga escala. A implementação de políticas públicas que incentivem a colaboração entre os setores da saúde humana, animal e ambiental também é essencial para otimizar os resultados no enfrentamento da resistência antimicrobiana.

Palavras-chave: Resistência Antimicrobiana. Mastite. One Health. Tratamentos Sustentáveis. Práticas Veterinárias.

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ABSTRACT: Antimicrobial resistance (AMR) in bovine mastitis has become an increasing concern for public and veterinary health, compromising the effectiveness of conventional treatments and raising management costs. Mastitis is primarily caused by Staphylococcus aureus and Escherichia coli, pathogens that have shown increasing resistance to common antibiotics such as penicillin and tetracycline. The One Health approach, integrating human, animal, and environmental health sectors, emerges as an effective strategy to combat resistance and improve treatment efficacy. This study systematically reviewed articles published between 2020 and 2025, utilizing PubMed, BIREME and SciELO databases, aiming to assess how the One Health approach impacts AMR in mastitis and explore sustainable therapeutic alternatives. A total of 19 articles meeting the inclusion criteria were selected, addressing the prevalence of AMR in mastitis pathogens as well as the application of vaccines and phytotherapies as alternatives to antibiotic use. Results showed that resistance primarily increased due to excessive antibiotic use, while the One Health approach was found promising in controlling resistance by integrating veterinary, public health, and environmental practices. Additionally, sustainable alternatives such as vaccines and phytotherapies proved effective in reducing resistance without introducing new resistance issues. This study concludes that the implementation of the One Health approach, combined with sustainable alternatives, offers an effective model for controlling antimicrobial resistance in bovine mastitis. However, it is important to highlight the scarcity of in-depth studies on the long-term efficacy and viability of sustainable therapeutic alternatives. The lack of robust data limits the application of these solutions in the field and emphasizes the urgent need for new studies to confirm their effectiveness on a large scale. The implementation of public policies encouraging collaboration among human, animal, and environmental health sectors is also essential to optimize outcomes in managing antimicrobial resistance.

Keywords: Antimicrobial Resistance. Mastitis. One Health. Sustainable treatments. Veterinary practices.

INTRODUCTION

Antimicrobial resistance (AMR) in bovine mastitis is an escalating issue that affects both public and veterinary health globally, particularly in countries with significant dairy production, such as Brazil. Mastitis is one of the most prevalent diseases in dairy cattle, with an incidence rate that can exceed 28% of the national herd, leading to annual economic losses exceeding R$ 6 billion, according to data from Embrapa (Globo Rural *et al.*, 2023; UFFS, 2017). This condition is primarily caused by pathogens such as *Staphylococcus aureus* and *Escherichia coli*, which have developed resistance to commonly used antibiotics like penicillin, tetracycline, and ampicillin, undermining the effectiveness of conventional treatments. The overuse of antimicrobials, especially during the dry period in cows, has accelerated resistance, further complicating disease control and increasing management costs (Okello *et al.*, 2023; Crespi *et al.*,2023).

AMR in bovine mastitis represents a critical gap in the scientific literature, as current solutions are proving insufficient in the face of increasing resistant strains. Whilst many studies have focused on the use of antibiotics and their limitations, few address an integrated solution that takes into account the human, animal, and environmental factors crucial to the spread of resistant strains. The One Health approach, which integrates these three aspects of health, emerges as an innovative strategy to mitigate antimicrobial resistance by considering its transmission between animals and humans. This approach enables a coordinated and effective response to the issue, contributing to the sustainability of disease management, such as mastitis, and promoting more responsible antimicrobial use practices (Li *et al.*, 2022). The novelty of this study lies in analyzing how integrating the health spheres can improve resistance control compared to conventional treatments while exploring sustainable therapeutic alternatives.

The dynamics of One Health approach involving the collaboration of human-animal-environment sectors in AMR remains unclear due to the dearth of data, well-defined and case-controlled studies. This impedes efforts targeted at controlling AMR in order to mitigate its health risks threat to the public. Sustainable alternatives such as vaccines, phytotherapies, and immunotherapies have shown promise in controlling mastitis without contributing to antimicrobial resistance. Studies suggest that vaccines can reduce the need for antibiotics, while plant-based treatments exhibit antimicrobial activity without increasing resistance (Okello *et al.*, 2023; Li *et al.*, 2022). However, the adoption of such alternatives faces challenges, including high costs and lack of adequate infrastructure for implementation. In this regard, collaboration between public health, veterinary, and environmental sectors is crucial to overcoming these barriers and promoting sustainable management practices.

The main objective was to analyze and synthesize studies on the effectiveness of the One Health approach in controlling antimicrobial resistance (AMR) in bovine mastitis, comparing it to conventional treatments and exploring sustainable alternatives. This study aims to assess the effectiveness of the One Health approach in the treatment of bovine mastitis, comparing it to conventional treatments in order to understand its practicability in veterinary practice. Additionally, it seeks to explore sustainable therapeutic alternatives for controlling antimicrobial resistance, providing valuable data that can contribute to public health and policy strategies integrating these different sectors. The research stands out by integrating a holistic

analysis of antimicrobial resistance, considering the interactions among various components of the health ecosystem, contributing key recommendations as well as specific action plans and interventions for combating AMR.

METHODOLOGY

The methodology of this study follows the guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), a standardized approach to ensure transparency and replicability in systematic reviews (Moher *et al.*, 2016).

The PICO strategy (Population, Intervention, Comparison, and Outcome) is a useful tool for structuring research questions (Moher *et al.*, 2016). For the question "What is the impact of sustainable therapeutic alternatives, such as phytotherapeutics, vaccines, and nanotechnology, on antimicrobial resistance in bovine mastitis, considering the One Health approach?", the Population is dairy cows with mastitis; the Intervention involves sustainable therapies; the Comparison is with conventional treatments; and the Outcome is the reduction of antimicrobial resistance. The One Health approach will be considered, integrating human, animal, and environmental health.

Search strategy

A comprehensive search of the PubMed and SciELO databases were carried out to retrieve list of primary articles (not reviews) published between 2020 - 2025 that addressed antimicrobial resistance in *Staphylococcus aureus* and *Escherichia coli*, the main pathogens causing mastitis, as well as articles discussing sustainable therapeutic alternatives and the application of the One Health approach and sustainable treatment alternatives. The search strategy used in BIREME, PubMed and SciELO databases, known for their breadth and quality in the fields of public health, veterinary medicine, and environmental sciences, used a combination of Medical Subject Headings (MeSH/DECS) related to antimicrobial resistance and bovine mastitis “Antimicrobial resistance,” “Mastitis,” and “One Health” with the Boolean operator AND.

Criteria for inclusion

Primary data sources were selected from the PubMed, BIREME and SciELO, which contain a large number of relevant scientific articles. PubMed is a globally recognized database focusing on biomedical and health sciences, while SciELO and BIREME are databases that includes Latin American scientific journals, with a strong emphasis on regional studies. The search was refined to ensure that the selected articles were relevant to the research question and within the defined temporal and geographic scope. The selected studies were published in English, Spanish, or Portuguese.

Criteria for exclusion

Review articles, master's or doctoral theses, and articles that did not address antimicrobial resistance in bovine mastitis or did not cover the application of the One Health approach were excluded. Articles that did not provide primary data on treatment effects or were available only in languages other than English, Spanish, or Portuguese were also excluded. Literature reviews were excluded, as although they could offer meta-analyses, they do not meet the objective of reviewing primary data on specific interventions for controlling resistance in mastitis, and they carry publication bias risks that could compromise the analysis.

Data extraction and risk-of-bias assessment

After searching the databases, the titles and abstracts of the articles were independently analyzed by two reviewers. In cases of disagreement, a third reviewer was consulted to resolve the divergence. Articles that met the inclusion criteria were selected for full analysis. The quality of the studies was assessed using the RoB 2.0, to ensure the studies included were of high quality and met the necessary transparency and methodological rigor standards.

Data extraction was carried out using a standardized form, which included information on authors, year of publication, study objectives, study type, interventions performed, main results, and conclusions. For the comparative analysis, data were extracted on the effectiveness of the One Health approach versus conventional treatments, as well as sustainable therapeutic alternatives such as vaccines, herbal treatments, and management strategies. The data extraction criteria were defined based on the relevance of the articles to the research question,

focusing on the effectiveness of the One Health approach, antimicrobial resistance, and sustainable alternatives.

The extracted data were synthesized qualitatively, with emphasis on the main findings of the studies. The comparison between the One Health approach, sustainable treatment alternatives and conventional treatments was made based on the treatment efficacy data and the observed impacts on antimicrobial resistance. Furthermore, sustainable alternatives were analyzed in terms of their effectiveness in reducing resistance and promoting more responsible management practices. A critical analysis of the studies was performed to assess the methodological quality, internal validity of the results, and the applicability of the findings to veterinary and public health practice. The implications for public health and veterinary policies were discussed, focusing on how the One Health approach can be implemented to improve the control of antimicrobial resistance in mastitis.

Table 1 contains the following data: study objectives, authors, country, study type, and risk of bias according to ROBINS-I, while **Table 2** addresses the following: methods of resistance evaluation, key results, and sustainable therapeutic alternatives.

Table 1.

Methodological framework and bias assessment in antimicrobial resistance research

Author, Year	Country of study	Study type	Objectives	Risk of bias according to ROBINS-I
Benites *et al.*, 2021	Brazil	Observational study	To evaluate the antimicrobial resistance profiles of *Staphylococcus* spp. isolated from bovine clinical mastitis, focusing on beta-lactams and gentamicin, and correlating phenotypic (in vitro susceptibility tests) and genotypic (molecular detection of resistance genes) characteristics.	Moderate risk.
Brito *et al*, 2024	Brazil	Cross-sectional study	To evaluate the antimicrobial susceptibility profiles of *Staphylococcus spp.* and *Streptococcus spp.* isolated from cows with infectious mastitis in dairy farms of São Luís, Maranhão, Brazil.	Moderate risk.
Crespi *et al.*, 2021	Argentina	Cross-sectional study	Determine antimicrobial resistance in *Staphylococcus* and *Streptococcus*	Low risk.

			isolated from milk of cows with mastitis and genetically characterize methicillin-resistant *Staphylococcus* (MRSA).	
de Oliveira *et al*., 2022	Brazil	Cross-sectional study	To identify the diversity of *Staphylococcus* spp. in subclinical mastitis in dairy herds in Piauí, Brazil, and evaluate the phenotypic and genotypic resistance profiles of these bacteria.	Moderate risk.
Đuričić *et al*., 2020	Croatia	Randomized experimental study	Evaluate the effects of clinoptilolite supplementation on intramammary infections and antimicrobial resistance.	Low risk.
Fidelis *et al*., 2024	Brazil	Observational study	To evaluate the biofilm formation capacity and antimicrobial resistance profiles of Staphylococcus aureus and Streptococcus uberis from cows with clinical and subclinical mastitis.	Moderate risk.
Forno-Bell *et al*., 2021	Chile	Experimental study	To investigate the efficacy of Aloe vera combined with antibiotics to treat bovine mastitis caused by S. aureus.	Moderate risk.
Kabui *et al*., 2024	Kenya	Cross-sectional study	To investigate the prevalence of clinical and subclinical mastitis in goats, identify associated risk factors, and antimicrobial resistance profiles	Low risk.
Li *et al*., 2022	China	Experimental study, laboratory resistance analysi	To analyze the antimicrobial resistance of E. coli strains isolated from bovine mastitis and the genetic correlations.	Low risk.
Nelli *et al*, 2022	Greece	Observational study	To investigate the antimicrobial and methicillin resistance patterns of *Staphylococcus aureus* and coagulase-negative staphylococci (CoNS) isolates from the mammary secretion of dairy goats, focusing on resistance to important antibiotics such as penicillin and methicillin.	Moderate risk.
Okello *et al*., 2023	United States	Longitudinal Study	The study aimed to evaluate the effect of dry cow therapy (DCT) on the antimicrobial resistance (AMR) profile of mastitis pathogens post-calving.	Low risk.
Rivera Aguayo et al., 2020	Chile	Experimental study	To evaluate the antimicrobial and antibiofilm efficacy of chitosan	Moderate risk.

			nanoparticles against Pseudomonas sp.	
Saeed *et al*., 2022	Malaysia	Observational study	To evaluate the prevalence of subclinical mastitis and antimicrobial resistance in Staphylococcus aureus isolated from cows with subclinical mastitis.	Moderate risk.
Song *et al*., 2024	China	Observational study	Investigate the antimicrobial resistance (AMR) profiles of common mastitis pathogens on dairy farms in China.	Low risk.
Tong *et al*., 2025	China	Experimental study	To evaluate the feasibility of hydrogels containing BLfcin-NPs in the treatment of mastitis, with an emphasis on controlled antibiotic release and resistance mitigation.	Moderate risk.
Yang *et al*., 2023	China	Original Research	To investigate the antimicrobial resistance and virulence profiles of staphylococci isolated from clinical bovine mastitis in Ningxia Hui Autonomous Region, China.	Moderate risk.
Zaghen *et al*., 2023	Italy	Epidemiological study	To analyze the epidemiology of antimicrobial resistance (AMR) genes in *Staphylococcus aureus* isolates from a public database in a One Health perspective, focusing on sample characteristics and sources of isolates.	Low risk.
Zhao *et al*., 2022	China	Experimental study	Identify antimicrobial resistance and virulence genes, evaluate antimicrobial resistance	Low risk.
Zouharova *et al*., 2024	Czech Republic	Cross-sectional study	To assess the antimicrobial susceptibility and resistance gene profiles of *Streptococcus uberis* isolated from bovine mastitis in Czech dairy farms and evaluate the development of antimicrobial resistance over five years (2019-2023).	Low risk.

Source: Author's own, 2025.

Table 2.

Methods of resistance evaluation, key results, and sustainable therapeutic alternatives

Author, Year	Methods of resistance evaluation	Main results	Sustainable therapeutic

			alternatives used
Benites *et al*., 2021	In vitro antimicrobial susceptibility testing and PCR/RT-PCR for detection and expression of resistance genes.	The study found high levels of antimicrobial resistance in *Staphylococcus* spp. strains isolated from bovine mastitis, particularly against penicillin, amoxicillin, and ampicillin (42.1% resistance). The most frequently detected resistance genes were femA and femB (75.4% of isolates). Resistance to gentamicin was also observed, with the aacA-aphD gene present in 50% of the resistant strains. The mecA gene, associated with methicillin resistance.	No specific sustainable therapeutic alternatives were used in the study.
Brito *et al*, 2024	Antimicrobial susceptibility testing by disk diffusion for 14 antimicrobials, with assessment of resistance to penicillin, amoxicillin, tetracyclines, and other antibiotics.	Antibiotic residues showed high resistance to penicillin and tetracyclines, with 32.65% of the strains resistant to more than 8 antibiotics simultaneously.	Rational use of antimicrobials, appropriate management practices, with recommendations for antimicrobial susceptibility testing.
Crespi *et al*., 2021	Disk diffusion test and agar dilution method for MIC evaluation, PCR for identification of resistance genes.	Coagulase-negative staphylococcus (CNS) strains showed resistance to penicillin (24.6%) and oxacillin (6.5%), while 3.2% of S. aureus strains were MRSA.	No specific sustainable therapeutic alternatives were used in the study.
de Oliveira *et al*., 2022	Disk-diffusion test and PCR for resistance genes such as blaZ, tetL, tetM, mecA, and vanB.	High resistance to penicillin (70%) and ampicillin (61.8%) in the isolates, with the presence of the blaZ gene in 60.9% of the samples.	No specific sustainable therapeutic alternatives were used in the study.
Đuričić *et a*l., 2020	Antibiotic susceptibility testing, microbiological cultures.	Cows in the CPL group had a 1.96 times lower risk of intramammary infection.	Clinoptilolito vibroativado (CPL)
Fidelis *et al*., 2024	Disk-diffusion test and microplate method for biofilm formation.	57.4% of S. aureus isolates and 53.8% of S. uberis isolates formed biofilms, with resistance to penicillin (92.9%) and ampicillin (50.8%) in S. aureus, and resistance to oxacillin (80.6%) and penicillin (80.6%) in S. uberis.	No specific sustainable therapeutic alternatives were used in the study.
Forno-Bell et al. 2021	Minimum inhibitory concentration (MIC) assessment, pharmacokinetic analysis of treatments, and calculation of efficacy index.	The combination of Aloe vera with antibiotics (cloxacillin and ceftiofur) showed good therapeutic efficacy rates with favorable T > MIC values (23.29 ± 6.89h for Aloe + cloxacillin and 27.5 ± 2.57h for Aloe + ceftiofur).	Aloe vera (alcoholic extract) combined with cloxacillin and ceftiofur.
Kabui *et al*., 2024	Disk diffusion test and PCR for resistance genes (mecA and blaTEM).	The prevalence of subclinical mastitis was 84.7%, with Staphylococcus aureus (22%) being the most prevalent pathogen.	No specific sustainable therapeutic

		Resistance to oxacillin was observed in up to 100% of the isolates.	alternatives were used in the study.
Li *et al*., 2022	Susceptibility tests to 13 common antibiotics, PCR for detection of resistance genes, Multilocus Sequence Typing (MLST).	Most E. coli strains were multidrug-resistant (MDR), with 72.5% of strains resistant to multiple antibiotics. The most prevalent resistance genes were aadA (62.5%) and tet(B) (60%).	Aloe vera (alcoholic extract) combined with cloxacillin and ceftiofur.
Nelli *et al*, 2022	Disk diffusion test, MIC (minimum inhibitory concentration) determination using VITEK 2 COMPACT, PCR for resistance genes, including mecA.	76.1% of the isolates were resistant to at least one antimicrobial, with predominant resistance to benzylpenicillin.	No specific sustainable therapeutic alternatives were used in the study.
Okello *et al*., 2023	Susceptibility testing to 13 common antibiotics, with resistance gene detection and genetic typing by Multilocus Sequence Typing (MLST) for Escherichia coli samples.	Most E. coli samples (75%) were multidrug-resistant, with notable resistance to cephazolin (77.5%), sulfamethoxazole (55%), and ampicillin (52.5%).	No specific sustainable therapeutic alternatives were used in the study.
Rivera Aguayo *et al*., 2020	MIC, MBC, disk diffusion test, and biofilm inhibition test.	Chitosan nanoparticles (CNPs) showed an MIC of 280 μg/mL and an MBC of 700 μg/mL, comparable to conventional antibiotics. CNPs demonstrated the ability to eradicate mature Pseudomonas sp. biofilms.	Chitosan nanoparticles (CNPs)
Saeed *et al*., 2022	Antimicrobial susceptibility tests (disk diffusion method), multiple antibiotic resistance (MAR) index, biofilm formation assays, and cell invasion assays.	31.4% of the samples showed subclinical mastitis; 16.5% of the samples had S. aureus resistant to multiple antimicrobials (penicillin, ampicillin, oxacillin).	No specific sustainable therapeutic alternatives were used in the study.
Song *et al*., 2024	Microdilution method, antimicrobial susceptibility test for different strains.	More than 75% of Staphylococcus aureus and CNS samples showed resistance to penicillin. Less than 10% of all samples showed resistance to other antimicrobials such as amoxicillin/clavulanate and rifaximin.	No specific sustainable therapeutic alternatives were used in the study.
Tong *et al*., 2025	Bacterial inhibition zone assessment and bacterial growth inhibition at different time intervals.	BLfcin-NP hydrogels showed higher antimicrobial activity compared to hydrogels without nanoparticles.	Thermosensitive hydrogels with bovine lactoferricin (BLfcin) loaded in chitosan nanoparticles.
Yang *et al*., 2023	Antimicrobial susceptibility testing (disk diffusion combined with E-test method) and PCR for resistance and virulence genes.	High antimicrobial resistance in S. aureus and coagulase-negative staphylococci, with resistance to penicillin, erythromycin, and tetracycline.	No specific sustainable therapeutic alternatives were used in the study.

Zaghen *et al.*, 2023	Antibiotic resistance testing, Cluster Analysis	Identified clusters with specific ARG patterns linked to human and non-human sources.	No specific sustainable therapeutic alternatives were used in the study.
Zhao *et al.*, 2022	Broth microdilution method, PCR for resistance and virulence gene detection	S. agalactiae was 100% resistant to ≥3 of the 16 antimicrobial agents tested, with resistance to oxacillin, tetracycline, erythromycin, clindamycin, and gentamicin.	No specific sustainable therapeutic alternatives were used in the study.
Zouharova *et al.*, 2024	Broth microdilution, whole-genome sequencing	High resistance to tetracycline (59%), streptomycin (38%), and clindamycin (29%); intermediate resistance to ampicillin (44%) and penicillin (18%)	No specific sustainable therapeutic alternatives were used in the study.

Source: Author's own, 2025.

RESULTS

The initial search in the PubMed and SciELO databases, using the keywords "Antimicrobial resistance," "Mastitis," and "One Health," yielded 418 articles. After applying temporal filters, restricting studies to those published between 2020 and 2025, and considering articles in Portuguese, English, and Spanish, the number of articles was reduced to 265. This initial filtering aimed to ensure the relevance and timeliness of the selected studies. Next, titles and abstracts were reviewed, leading to the exclusion of 114 articles were excluded as they directly address antimicrobial resistance in mastitis, 97 for being literature reviews, and 15 for being duplicates. As a result, the number of eligible studies for analysis was reduced to 39.

After a thorough analysis of the full texts, 19 articles were selected for inclusion in the final research base. These studies were deemed appropriate to answer the research question, meeting the inclusion criteria and providing relevant data on antimicrobial resistance in mastitis, comparing the One Health approach with conventional treatments, and exploring sustainable alternatives. The flowchart of the study selection process, which clearly illustrates all stages of the search and filtering, is shown in Figure 1.

Upon analyzing the studies, it is observed that all mention sustainable therapeutic alternatives, but not all of them specifically use these approaches. Some studies refer to alternatives such as activated clinoptilolite, aloe vera combined with antibiotics (cloxacillin and ceftiofur), chitosan nanoparticles, and thermosensitive hydrogels with bovine lactoferricin,

loaded in chitosan nanoparticles. However, most studies do not specify sustainable therapeutic alternatives. These observations highlight the gap in implementing sustainable alternatives in bovine mastitis treatments, emphasizing the need for further research to explore and evaluate such alternatives in clinical contexts.

The studies analyzed are distributed across various countries, with China leading, representing 26.3% of the studies. Brazil follows with 21.1%, while Chile appears at 10.5% . Other countries such as Argentina, Croatia, Kenya, Greece, the United States, Malaysia , Italy, and the Czech Republic each account for 5.3% of the studies. This geographic diversity reflects the global scope of research on antimicrobial resistance in bovine mastitis, although the studies are more concentrated in China and Brazil. After counting the studies, it was observed that the most used methodologies were observational experimental and cross-sectional studies, each with 5 occurrences, representing 26.3% each. On the other hand, randomized studies, original research, epidemiological studies, and longitudinal studies had only 1 occurrence each, representing 5.3% of the total.

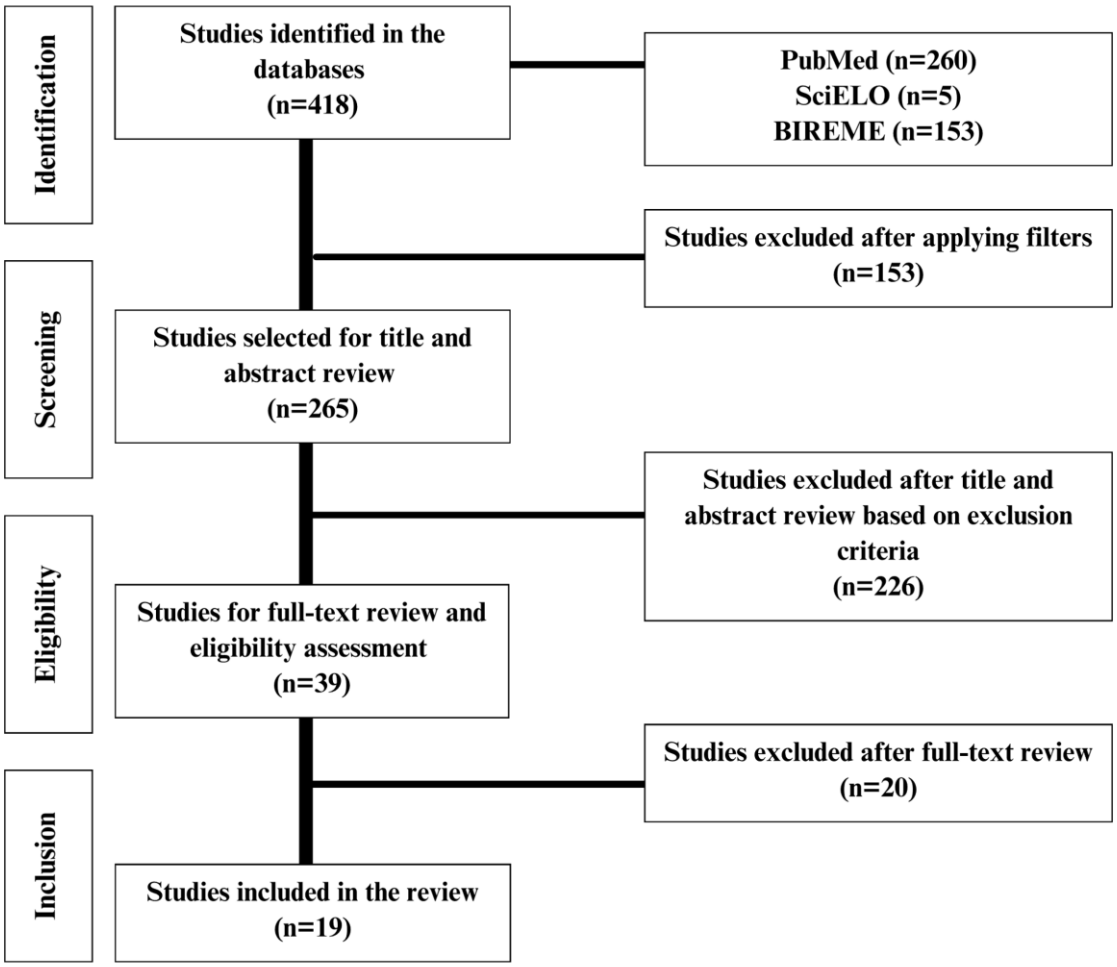
The studies reviewed consistently highlighted the growing issue of AMR in mastitis pathogens, particularly *Staphylococcus aureus* and *Escherichia coli*, which showed high resistance rates to common antibiotics such as penicillin, tetracycline, and ampicillin. Zhao *et al.* (2023) and Okello *et al.* (2023) in their studies reported that over 50% of *S. aureus* strains were resistant to multiple antibiotics, complicating treatment efforts.

The One Health approach was shown to be an effective strategy for managing AMR in mastitis. Research by Okello *et al.* (2023) and Crespi *et al.* (2022)confirmed that the integration of human, animal, and environmental health significantly improved the management of antimicrobial resistance, with coordinated efforts leading to a reduction in resistant strain transmission between animals and humans.

Several studies, including those by Crespi *et al.* (2022) and Zhao *et al.* (2023), explored alternative, sustainable treatments like vaccines, herbal therapies, and immunological treatments. These alternatives have been shown to reduce reliance on antibiotics, without contributing to further resistance.

Figure 1.

Flowchart of the study selection process from the databases



Source: Author's own, 2025.

DISCUSSION

Antimicrobial resistance (AMR) in bovine mastitis has become an increasing challenge for both public and veterinary health, mainly due to the indiscriminate use of antibiotics in treating this disease. Mastitis is one of the most common and costly conditions on dairy farms, affecting both animal health and milk production. Numerous studies highlight the growing resistance of pathogens such *as Staphylococcus aureus* and *Escherichia coli* to commonly used antibiotics such as penicillin, oxacillin, tetracycline, and ampicillin (Okello *et al.*, 2023; Li *et al.*,

2022; Brito; Costa, 2024). In this context, the One Health approach, which considers the interdependence between human, animal, and environmental health, emerges as an effective strategy to mitigate the spread of resistance and promote more sustainable treatments.

The use of antibiotics in the treatment of mastitis has limited effectiveness due to antimicrobial resistance, which increases with continuous use, especially of broad-spectrum antibiotics. Researchers have indicated that the use of antimicrobials during the dry period in cows is associated with increased resistance *in Staphylococcus aureus* and *Escherichia coli* (Okello *et al*., 2023). Other studies also highlight that more than 50% of S. aureus strains are resistant to multiple antibiotics, compromising conventional treatments and highlighting the need for alternatives that do not promote resistance (Brito; Costa, 2024). Compared to conventional treatments, alternative therapies such as vaccines and phytotherapeutics have shown potential. However, the evidence supporting the efficacy of phytotherapeutics needs to be strengthened, as current results have not been conclusive in all contexts, especially when compared directly to antibiotics (Saeed *et al*., 2024).

Additionally, *S. aureus* has the ability to form biofilms and invade epithelial cells of the bovine mammary gland, complicating treatment because antibiotics are less effective against bacteria in biofilms. The invasion of epithelial cells contributes to persistent infections and recurring reinfections (Saeed *et al*., 2024; Fidelis *et al*., 2024; de Oliveira *et al*., 2022). In this regard, a study reveals that certain plants, such as Minthostachus verticillate, showed efficacy in controlling mastitis by affecting bacterial biofilm formation. Furthermore, the use of bacteriocins such as Nisin, combined with nanoparticles, emerged as an effective alternative for treating multi-resistant Staphylococcus strains and other mastitis-related infections. Additionally, chitosan nanoparticles have proven to be highly effective in inhibiting biofilm formation and eradicating mature biofilms of *Pseudomonas sp*., a pathogen notorious for its resistance to conventional antibiotic treatments. The results show that the nanoparticles had a minimum inhibitory concentration (MIC) of 280 μg/mL and a minimum bactericidal concentration (MBC) of 700 μg/mL, values that are comparable to or even higher than conventional antibiotics used in bovine mastitis treatment (Rivera *al*., 2020).

Moreover, the economic viability of sustainable alternatives, such as vaccines and phytotherapeutics, remains a critical concern. While these alternatives may offer a more sustainable long-term solution, their high costs and the infrastructure required for their

implementation present significant barriers in many regions (Brito; Costa, 2024). Resistance is also associated with genes such as blaZ and mecA, which make treatments more challenging. Other research shows that *E. coli* resistance due to the presence of these genes compromises the effectiveness of antibiotics (Li *et al.*, 2022). The zoonotic transmission of resistant pathogens between animals and humans is a growing concern, as confirmed by studies emphasizing the importance of integrated practices and the responsible use of antimicrobials (Okello *et al.*, 2023; Benites *et al.*, 2021). However, there is still a lack of research on how these resistant strains interact at the human-animal-environment interfaces, and more study is needed to fully understand this dynamic and its broader implications for public health.

The One Health approach, which integrates human, animal, and environmental health, is crucial for addressing antimicrobial resistance (AMR) in bovine mastitis. Studies such as those by Okello et al. (2023) show that by considering the impacts of resistance across all sectors, more effective and coordinated solutions can be implemented. Antibiotic resistance does not occur in isolation, and efforts to combat it must involve public health, veterinary, and environmental professionals working together to reduce the spread of resistant strains. The integration of these sectors can lead to more effective resistance management, improving animal health monitoring and infection prevention (Zouharova *et al.*, 2023). However, the full potential of the One Health approach can only be realized if there is more collaboration between disciplines and countries, especially in regions with limited resources.

Given the rising resistance to conventional antibiotics, exploring sustainable alternatives is essential. Researchers suggest that vaccines and immunotherapies could play a key role in treating mastitis, reducing reliance on antibiotics (Okello *et al.*, 2023). Additionally, the use of phytotherapeutics is discussed as a promising alternative, as these natural treatments have antimicrobial properties that do not exacerbate resistance. The search for sustainable solutions involves not only the use of alternative treatments but also improving farm management practices, such as hygiene and infection control (Zhao *et al.*, 2022). The challenge lies in evaluating the long-term economic viability of these alternatives, especially on small farms where financial constraints hinder the adoption of such solutions.

Moreover, a study investigating the effect of dietary supplementation with vibroactivated clinoptilolite on the intramammary microbiology of dairy cows showed that the group receiving clinoptilolite (CPL) supplementation had a significantly lower risk of

intramammary infection compared to the control group. The risk of infection in cows in the control group was 1.96 times higher than in the CPL group (odds ratio = 1.96; p = 0.0031). The most frequently isolated pathogens in both groups were Staphylococcus aureus, coagulase-negative Staphylococcus (CNS), and Streptococcus uberis. In the CPL group, nine mastitis-causing agents were isolated from 27 quadrants, whereas in the control group, 13 pathogens were isolated from 59 quadrants. Clinoptilolite has antimicrobial and immunomodulatory properties that contribute to cow health and can be a viable option to complement traditional treatments, as well as promote more sustainable practices in bovine mastitis management (Đuričić *et al.*, 2023).

Authors report that vaccination against Staphylococcus aureus significantly reduced mastitis incidence in dairy cows, offering an effective and long-lasting solution (Crespi *et al.*, 2021). Additionally, plant extracts such as Echinacea purpurea have shown significant antimicrobial activity against mastitis pathogens without the adverse effects associated with conventional antibiotics. Other authors suggest that the application of sustainable therapeutic alternatives, such as using Aloe vera in intramammary formulations combined with antibiotics, could be an effective strategy to control resistance without exacerbating the situation (Forno-Bell *et al.*, 2021).

Moreover, authors have shown that hydrogels composed of BLfcin-NPs have a number of favorable characteristics for mastitis treatment, such as good biocompatibility, significant antimicrobial activity against Staphylococcus aureus and Escherichia coli, and the ability to release the antibacterial agent in a controlled manner. Analysis of the results showed that the hydrogel with BLfcin nanoparticles exhibited an inhibition zone of 17.15 ± 0.11 mm against E. coli and 16.63 ± 0.72 mm against S. aureus, significantly higher than the hydrogel containing BLfcin without nanoparticles (8.35 ± 0.34 mm for E. coli and 7.90 ± 0.25 mm for S. aureus). These data indicate that the combination of BLfcin with chitosan nanoparticles enhances antimicrobial activity and offers more efficient and prolonged antibiotic release (Tong *et al.*, 2025).

These alternatives could be crucial in controlling mastitis, especially in the context of increasing resistance (Li *et al.*, 2022). However, large-scale trials and more robust data are needed to determine their effectiveness in a wider range of conditions and to directly compare them with conventional antibiotic treatments.

Antimicrobial resistance affects both public and animal health. Studies show that resistant strains of Staphylococcus aureus can be transmitted from cows to humans, increasing the risk of resistant infections. This also impacts animal welfare, as untreated infections lead to suffering and reduced milk production, in addition to increasing the costs of mastitis treatment (Okello *et al*., 2020; Zhao *et al*., 2022; Nelli *et al*., 2022). The One Health approach, integrating human, animal, and environmental health, offers an opportunity to address these issues more comprehensively. Public health initiatives focused on reducing AMR should prioritize the interconnectedness of these sectors, leveraging intersectoral collaboration to minimize the risk of transmission and improve responses to outbreaks of resistance.

Controlling resistance requires sustainable strategies such as responsible antibiotic use, improvements in farm sanitation, and continuous monitoring. Robust surveillance programs integrating resistance data can enhance the fight against antimicrobial resistance (Zaghen *et al*., 2023). It is recommended to rotate antibiotics and use alternative therapies such as vaccines and phytotherapeutics to reduce resistance (Crespi *et al*., 2021). However, more evidence is needed on the cost-benefit relationship and scalability of these alternative treatments, especially in resource-limited settings.

Antimicrobial resistance is a global concern that affects both animals and humans, posing a significant public health risk. Researchers highlight that resistant strains can be transmitted to humans, exacerbating the problem. The One Health approach, integrating public health and veterinary efforts, can help contain this spread (Yang *et al*., 2023). However, challenges persist in implementing One Health frameworks globally, especially in underdeveloped regions where infrastructure is limited.

Implementing the One Health approach is crucial in managing antimicrobial resistance (Yang *et al*., 2023). Studies suggest that public policies encouraging collaboration between public health, veterinary, and environmental sectors can significantly reduce resistance. Applying this integrated approach can improve responses to outbreaks and control the spread of resistant strains (Kabui *et al*., 2024; Li *et al*., 2022). Effective policies, both nationally and internationally, are needed to encourage collaboration between sectors and ensure that the One Health model is adequately funded and supported.

Continuous surveillance of antimicrobial resistance is essential for detecting changes in resistance patterns and adapting treatments accordingly. Research emphasizes the importance

of exploring new therapeutic alternatives and implementing monitoring systems to track the evolution of resistance. It is suggested that real-time resistance data could help optimize treatment regimens and allow for faster, more effective responses to antimicrobial resistance, preventing the spread of resistant strains (Brito; Costa, 2024; Li *et al*., 2022).

One study suggests that implementing good management practices, such as using separate towels to dry each goat's udders and improving hygiene on farms, could significantly reduce mastitis prevalence. It also highlights the need for interventions to improve antimicrobial resistance control, such as educating farmers on prudent antibiotic use and adopting early diagnostic methods like the California Mastitis Test (CMT) (Song *et al*., 2024).

In summary, antimicrobial resistance in bovine mastitis is a complex problem that requires an integrated and sustainable approach (Kabui *et al*., 2024).. Using alternatives such as vaccines, phytotherapeutics, and immunotherapies, combined with responsible antibiotic management, may be the key to combating resistance and ensuring long-term treatment efficacy. The One Health approach, involving the veterinary, public health, and environmental sectors, is crucial in the fight against antimicrobial resistance in bovine mastitis. Collaboration between these sectors can reduce the spread of resistant strains, promote responsible antibiotic use, and encourage the development and implementation of sustainable therapeutic alternatives.

The search for studies directly addressing the issue of antimicrobial resistance in bovine mastitis, especially with a focus on the "One Health" integrated approach, has proven to be a significant challenge. Although there is a substantial number of articles related to bacterial resistance in mastitis, the interconnection between human, animal, and environmental health, as outlined by the "One Health" model, is still limited in the literature. More primary studies need to be conducted to fill this knowledge gap, allowing for a better understanding of the dynamics of antimicrobial resistance in various contexts. Moreover, it is essential that these studies consider integrated management practices and sustainable therapies to provide more effective solutions, reducing the reliance on conventional antibiotics and promoting safer and more feasible alternatives for treating bovine mastitis.

FINAL CONSIDERATIONS

Antimicrobial resistance (AMR) in bovine mastitis is a growing concern, not only for public health but also for veterinary health and the sustainability of agricultural practices. The indiscriminate use of antibiotics has favored the rise of resistant strains, compromising the effectiveness of conventional treatments. The increasing resistance of pathogens like Staphylococcus aureus and Escherichia coli to the most commonly used antibiotics calls for an urgent reflection on sustainable therapeutic alternatives, such as vaccines, phytotherapeutics, and bacteriophage therapies, which have shown promising potential in controlling mastitis.

The One Health approach, which integrates human, animal, and environmental health, emerges as an effective strategy to mitigate the spread of antimicrobial resistance. However, its implementation requires greater involvement between public health professionals, veterinarians, and environmentalists, as well as collaboration between countries, especially in resource-limited regions. Controlling antimicrobial resistance also involves adopting more responsible antimicrobial use practices and strengthening surveillance programs, which will allow for faster and more effective interventions.

While alternatives like vaccines and therapies based on natural products show great potential, more studies and large-scale clinical trials are needed to prove their efficacy in different contexts. Additionally, the economic viability of these solutions must be considered, especially in small farms, where costs are a limiting factor. Antimicrobial resistance in bovine mastitis requires an integrated, coordinated, and innovative approach, with collaboration across various sectors of society.

The analysis of antimicrobial resistance in bovine mastitis, with a focus on the "One Health" integrated approach, reveals a significant gap in the literature. While there are numerous studies on bacterial resistance in this context, few directly address the interrelationship between human, animal, and environmental health. The lack of primary research that considers this integration hinders the application of effective and sustainable strategies for controlling resistance. To improve practices and ensure more effective outcomes, it is essential to invest in more studies that investigate the impact of antimicrobial resistance holistically, considering both management practices and sustainable therapeutic alternatives. Such studies will help develop safer solutions and reduce reliance on antibiotics, promoting more effective treatment of bovine mastitis.

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