REVIEW ARTICLE

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Effect of bovine subclinical mastitis on milk production and economic performance of Brazilian dairy farms*

Efeito da mastite subclínica bovina sobre a produção de leite e desempenho econômico de fazendas leiteiras brasileiras

Juliano Leonel Gonçalves[1,2]; Gustavo Freu[1]; Breno Luís Nery Garcia[1]; Melina Melo Barcelos[1]; Bruna Gomes Alves[1]; Renata de Freitas Leite[1]; Camylla Pedrosa Monteiro[1]; Cristian Marlon de Magalhães Rodrigues Martins[1]; Tiago Tomazi[1]; Henk Hogeveen[3]; Marcos Veiga dos Santos[1]

[1]Universidade de São Paulo, Faculdade de Medicina Veterinária e Zootecnia, Departamento de Nutrição e Produção Animal, Pirassununga – SP, Brazil
[2]Michigan State University, College of Veterinary Medicine, Department of Large Animal Clinical Sciences, East Lansing – MI, USA
[3]Wageningen University, Business Economics Group, Wageningen, The Netherlands

ABSTRACT

This review summarized the significant results from Brazilian studies published in peer-reviewed scientific papers about the effect of bovine subclinical mastitis (SM) on economic performance and milk production. Different approaches were considered for (i) disease detection (indirect measurement of somatic cell count (SCC) and directly using microbiological culture) and (ii) milk sampling strategy (mammary quarters, composite cow samples, and bulk milk tank). Globally, bovine mastitis is the most common disease of dairy herds, and the subclinical presentation is the most frequent. Dairy farmers usually underestimate the economic losses associated with SM because no visual changes in milk and quarters, udder, and systemic symptoms are observed. SM reduces milk yield and quality, reducing dairy herds' profitability. The estimation of losses depends on the causative pathogen, the lactation stage, and the parity of affected cows. Thus, estimating the economic caused by SM in milk production and economic performance in dairy herds can be used to decide which mastitis control strategies to adopt. Mastitis control involves adopting specific measures associated with the characteristics of each herd, the period of the highest frequency of cases, the transmission form, and the profile of the pathogens involved in cases of intramammary infection. Thus, using individual SCC, the microbiological identification of pathogens causing SM, adopting efficient drying-off protocols, and other management practices are essential for mastitis control, improved milk quality, and greater profitability of dairy herds.

Keywords: Subclinical mammary infections. Alteration of milk composition. Indirect cost. Milk loss. Financial loss.

RESUMO

O objetivo deste artigo de revisão foi compilar os principais resultados obtidos em estudos brasileiros publicados em periódicos indexados, relacionados ao efeito da mastite subclínica (MS) sobre a produção e a rentabilidade de rebanhos leiteiros. Para isso, foram consideradas duas abordagens: (i) diagnóstico da mastite [com base na contagem de células somáticas (CCS) e na cultura microbiológica] e, (ii) estratégia de amostragem do leite (quartos mamários, amostras compostas de vacas e do tanque de rebanhos). A MS é a forma mais frequente de mastite em fazendas leiteiras, mas nem sempre seu impacto é compreendido adequadamente. A ausência de alterações visuais do leite, nos quartos mamários e/ou sistêmicas nas vacas acometidas dificulta o diagnóstico da MS, diminuindo a percepção das perdas e, consequentemente, levando os produtores a subestimarem os impactos na produção de leite e na rentabilidade dos rebanhos. O impacto da MS sobre a produção de leite e o desempenho econômico das fazendas leiteiras depende do patógeno causador da doença, do estágio da lactação e do número de parições das vacas. Assim, a estimativa das perdas causadas pela MS sobre produção de leite e o desempenho econômico das fazendas leiteiras pode ser usada para a tomada de decisões de implementação de medidas de controle da MS. De modo geral, o controle da MS requer a implantação de medidas especificas para cada rebanho, de acordo com o período em que há maior frequência de casos, o perfil de transmissão da doença e tipo de agente envolvido nos casos de mastite. Por isso, o monitoramento do rebanho pelo uso da CCS das

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vacas do rebanho, diagnóstico microbiológico de agentes causadores de MS, o uso de protocolos de secagem eficientes e medidas adicionais de manejo, são essenciais para o controle da mastite, qualidade do leite e desempenho econômico de fazendas leiteiras.

Palavras-chave: Infecções mamárias subclínicas. Alteração na composição do leite. Custo indireto. Perda de leite. Perda financeira.

Correspondence to:
Marcos Veiga dos Santos
Universidade de São Paulo, Faculdade de Medicina Veterinária e Zootecnia, Departamento de Nutrição e Produção Animal
Av. Duque de Caxias Norte, 225, Campus Fernando Costa, Jardim Elite
CEP: 13635-900, Pirassununga – SP, Brazil
e-mail: mveiga@usp.br

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Introduction: The Importance of Mastitis in Dairy Herds

Mastitis is the most critical disease affecting dairy cows worldwide (Ruegg, 2017), increasing the total production costs and reducing dairy herds' economic and productive efficiency. Most of the time, the disease is caused by bacterial infections (Ruegg, 2017; Tomazi et al., 2018), which result from an invasion of the mammary gland through the teat canal (Hogan & Smith, 2003). As a result, bacterial intramammary infections alter the milk-secreting mammary epithelial cells, negatively affecting milk quality in dairy herds (Gonçalves et al., 2021; Le Roux et al., 2003).

Mastitis can be classified according to the manifestation of signs in clinical (visible signs of changes in milk and udder) and subclinical (no visual changes in the milk, udder, and systemic, but with increased somatic cell count (SCC) and compositional changes (De Vliegher et al., 2018; Forsbäck et al., 2010; Pumipuntu et al., 2017). Concerning producers' perception of the disease's cost, most underestimate the losses caused by subclinical mastitis (SM). According to Pitkälä et al. (2004), SM can affect 20-50% of lactating cows in dairy farms, being the most common form of mastitis (Forsbäck et al., 2009).

Defining the terms expense and loss is necessary to estimate the cost of mastitis. Expense is any additional outlay from mastitis, i.e., expenses with intramammary antibiotics and disposal of milk with antibiotics residues. Loss is a potential not reached because of mastitis, such as reduced milk production and loss of bonuses for quality payment (Gonçalves et al., 2018a). Disbursements are associated with clinical mastitis, while losses are associated with subclinical cases.

Dairy farmers have the perception that direct losses (e.g., discarding milk, involuntary culling of cows and medicines) are more significant than the reduction in milk production potential of dairy cows, which weighs heavily on the economic impact caused by mastitis (Guimarães et al., 2017). However, this perception of producers about the costs of mastitis is based only on the amounts disbursed, which leads to an underestimation of the damage caused by the disease and, consequently, to a lower incentive to implement control measures since the losses are not perceived (Hogeveen et al., 2019).

Earlier investigations evaluated divergent estimates for the economic impact of mastitis, mainly because of the diversity of methodologies used (Hagnestam-Nielsen et al., 2009; Huijps & Hogeveen, 2007; Tesfaye et al., 2010; Van Asseldonk et al., 2010). Most of the previous studies evaluated the disbursements associated with clinical mastitis because of the greater perception by the producer of the losses, as mentioned above. On the other hand, until the last decade, the losses caused by SM had been evaluated based on simulations and bibliographic review (Huijps et al., 2008; Petrovski et al., 2006; Seegers et al., 2003).

Loss assessments have been performed using SCC to estimate the reduction in milk production associated with SM (Dürr et al., 2008; Gonçalves et al., 2018b). However, these assessments must consider factors such as animal breed, the number and the stage of lactation, which affect the intensity of production losses and changes in milk composition caused by mastitis (Dürr et al., 2008; Gonçalves et al., 2018b). In a pioneering study, the effect of the lactation stage was considered in the model. Therefore, the milk loss was lessened for primiparous cows (0.6 Kg/d) compared to multiparous cows (3.3 Kg/d) (Coldebella et al., 2003). A recent study evaluated SM loss according to the type of mastitis-causing pathogen at the cow level. In that study, the milk production of cows with SM was reduced by up to 24.5% and the production of solids by 22.4% (Martins et al., 2020).

Losses caused by SM on milk production may vary according to the assessment method, SM detection test (indirectly by SCC or directly by type of pathogen according to the microbiological culture - MC), the group of causative microorganisms (environmental, contagious, or minor), stage and number of lactation. Cows with intramammary infections caused by environmental and contagious pathogens decrease milk production by 0.6 and 0.7 Kg/milking, respectively (Gonçalves et al., 2018a, 2018b). On the other hand, no reduction of milk yield was observed when the comparison of mammary quarters infected by minor pathogens (e.g., non-*aureus Staphylococcus* and *Corynebacterium* spp.) with healthy contralateral mammary quarters were made (Gonçalves et al., 2016, 2018a; Tomazi et al., 2015).

The estimate of losses is crucial for decision-making in the herds, as it justifies implementing mastitis control measures. Therefore, we reviewed the central studies developed in Brazil based on the effect of bovine SM on the economic performance of dairy farms and milk production given different approaches: (i) detection of the disease (indirect, SCC vs. direct, type of pathogen) and (ii) milk sampling strategy (mammary quarter, cow, and herd), focused on the economics of SM, specifically under Brazilian dairy farms conditions.

Effect of Bovine Subclinical Mastitis at the Herd Level

One way to measure the impact of SM on economic performance is to consider the indicators at the herd level using mathematical simulations (Dillon et al., 2015; Geary et al., 2013). A recent study evaluated the association between bulk tank milk SCC (BTSCC) of 543 herds in Minas Gerais and the economic performance indicators (Gonçalves et al., 2021), among which were income, profit margin, net margin, profit, break-even, and operating income. All economic indicators were evaluated and expressed per cow (US dollars/cow/year) and included: a) the effects of five different regions of Minas Gerais from 2015 to 2017; b) the classification of the herd sizes considering the number of lactating cows (<39 cows, ≥39 and ≤64, >64 and <100, >100); and c) average milk production in Kg cow/day (<14, ≥14 and <19, e ≥19; Gonçalves et al., 2021). The herds studied had an average of 82 lactating cows with an average production of 15.1 to 20.5 Kg/d. Most herds (94.6%) presented BTSCC >200,000 cells/mL, 37.8% had BTSCC from 200 to 400, 14.5% had BTSCC from 400 to 500, 25% had BTSCC from 500 to 750, and 1.3% had BTSCC >750 thousand cells/mL. BTSCC was negatively associated with revenue, gross margin, and yearly profit per farm and cow. On average, the farms obtained a gross margin of $678/cow/year and a profit of $227/cow/year when BTSCC was <200,000 cells/mL (Figure 1). In other words, a farm with 100 lactating cows and BTSCC <200,000 cells/ml, had a profit being 33.5% of annual gross margin. For each Log unit increase in BTSCC, the farmer's revenue decreased by $228/cow/year, and gross margin and profit decreased to $156/cow/year and $139/cow/year, respectively. Profit was negatively associated with BTSCC. The increase from 100,000 cells/mL to 750,000 cells/mL represented a negative profit of -$53.1/cow/year.

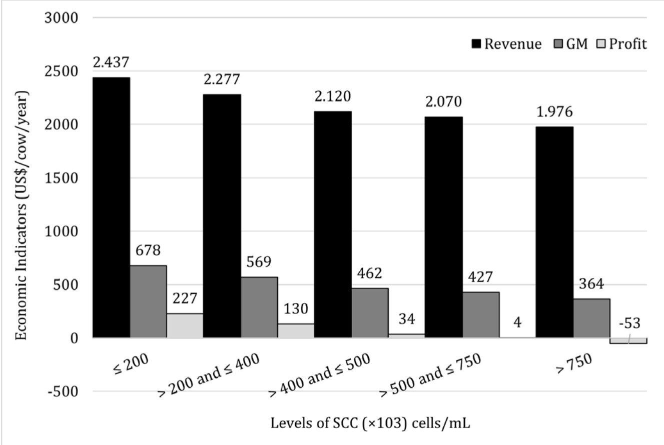

Figure 1 – Relation among economic indicators (revenue, GM = gross margin, and profit, estimated at US$ cow/year) according to BTSCC levels (× 1000) cells/mL. Adapted from Gonçalves et al. (2021).

This pioneering study showed the negative association between BTSCC and milk production, which resulted in lower profitability for dairy farms, similar to previous studies (Aghamohammadi et al., 2018; Geary et al., 2012). For each unit of increase in BTSCC, there was an average loss of 641 L cow/year (9.4%), considering a healthy cow when SCC ≤200.000 cells/mL with an average production of 6843.3 L (Gonçalves et al., 2021). In general, the loss of milk production associated with high BTSCC is often not easily perceived by farmers, while disbursements (fixed costs, dietary costs, for example) to keep a dairy cow producing are the same (Hogeveen et al., 2019).

It is estimated that the milk production loss represents 70 to 80% of the total costs associated with SM (Huijps et al., 2008). Therefore, studies on the association between economic indicators and the occurrence of mastitis help justify the need to implement measures to control the disease, especially for farmers with low production scale (Bezman et al., 2015; <39 lactating cows and <14 Kg milk/

cow/day), who are at greater risk of loss, and consequently, going out of dairy production business.

Effect of Bovine Subclinical Mastitis at the Cow Level

Somatic cell count is one of the most used indicators to estimate the occurrence of SM at the cow level in dairy farms (Busanello et al., 2017). SCC >200,000 cells/mL indicates subclinical intramammary infection (Dohoo & Leslie, 1991), resulting in milk yield loss (Dürr et al., 2008; Gonçalves et al., 2018a). Recently, a study estimated milk production losses associated with SM at the cow level (Gonçalves et al., 2018b). The study's main objectives were to estimate the SCC at which milk production losses start; (b) quantify milk production losses according to the SCC, according to the number and stage of lactation. A total of 232,937 dairy herd improvement data were used during five years (2010-2015), from 31,692 Holstein cows from 243 herds in Paraná, Brazil.

The cutoff point at which a reduction in milk production, even if negligible, associated with SCC was observed was 12,400 cells/mL for dairy cows (averages: first lactation: 32.2 Kg/day; second: 37.6 Kg/day and third: 38.7 Kg/day). Based on the linear regression coefficient of milk losses, an increase in SCC from 100,000 to 270,000 cells/mL (for each increase of a log unit of SCC) resulted in losses of - 0.7 kg/day for first lactation cows, -1.6 kg/day for second lactation cows, and -2.3 kg/day for third lactation cows (Gonçalves et al., 2018b). Figure 2 presents production losses (%) according to SCC groups (200, 400, 500, and 750,000 cells/mL) and lactation numbers. Similarly, a previous study estimated milk production losses of 0.6 and 3.3 kg/milk/day for primiparous and multiparous cows, respectively, with losses starting from SCC of 14,270 cells/mL (Coldebella et al., 2003). Milk production loss associated with increased SCC results from the mammary glands' inflammatory response to mastitis-causing pathogens (Halasa et al., 2009; Hogeveen et al., 2011; Huijps et al., 2008).

Another study evaluated 790 Holstein cows from six farms to evaluate the impact of chronic subclinical mastitis (CSM) caused by different groups of pathogens on milk production and quality at the cow level (Martins et al., 2020). The study enrolled 388 cows to evaluate milk yield and composition, SCC and, three milk samplings during two weeks were used to diagnose intramammary infection. According to the condition of the mammary gland, cows were grouped into four categories: healthy, SM, and CSM (culture-negative and culture-positive). Healthy cows produced more milk when compared with chronically infected cows that were culture-positive caused by minor (+5.2 kg/cow/day) and major pathogens (+7.1 kg/cow/day), respectively (Martins et al., 2020). Milk losses varied from 5.8 to 11.8 kg/cow/day according to the CSM type of pathogen (Figure 3). In summary, the milk production loss associated with CSM was 44.9% for Streptococcus like-bacteria; 35.3% for *Streptococcus agalactiae*; 27% for *Streptococcus dysgalactiae*; 26% for *Streptococcus uberis* and *non-aureus* Staphylococci, and 24.5% for *Staphylococcus aureus* (Martins et al., 2020). Instead, no reduction in milk yield was observed in cows with CSM caused by *Corynebacterium* spp. when compared to healthy cows (Martins et al., 2020).

In the same study, culture-positive cows with CSM had lower production of milk components in comparison to healthy cows (Martins et al., 2020). The lower production

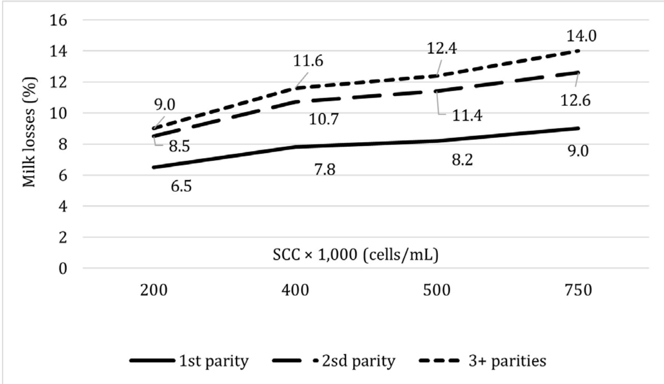

Figure 2 – Milk Production losses (%) according to SCC groups (200, 400, 500, and 750,000 cells/mL) and by lactation number. Adapted from Gonçalves et al. (2018b).

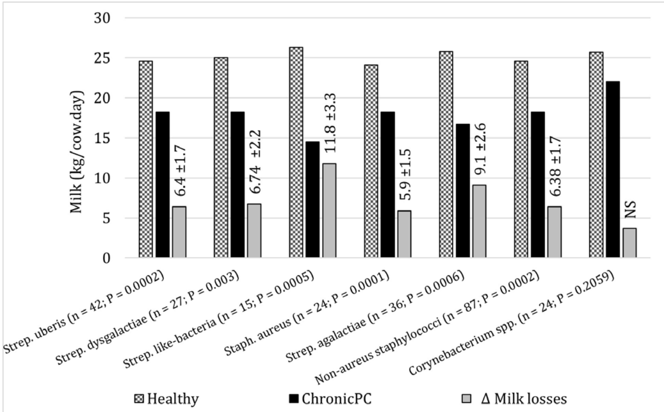

Figure 3 – Effect of culture-positive CSM (chronic-CP), presented by type of pathogen, on milk production, compared to healthy cows. * Δ milk loss estimated by the difference in milk production from healthy cows vs. culture-positive chronic cows (Chronic-CP) ± Standard error of the mean. *P<0.05. NS = not significant. Adapted from Martins et al. (2020).

of milk components (fat, lactose, non-fat solids, protein, and total solids) of cows with CSM depended on the type of pathogen and varied from 16.5 to 47.5% (Martins et al., 2020). França et al. (2017) reported that lactose content and crude protein were the most critical components of milk that suffer alteration with the increase of SCC. This relationship depends on the type of the pathogen. Other studies have also reported considerable losses in milk production and composition and have shown that the extent of these losses depends on the pathogen causing the disease (França et al., 2017; Wilson et al., 1997).

Effect of Subclinical Mastitis at the Udder Quarter Level

The evaluation of the impact of mastitis at the mammary quarters aimed at estimating the losses only in infected quarters. When composite milk samples are used to assess the effect of mastitis on milk yield, there may be a diluting effect of healthy mammary quarters (Blum et al., 2014; Forsbäck et al., 2009). Therefore, evaluation of mastitis at the mammary quarter level can minimize some of the confounding factors sometimes present in cow and herd-level approaches (Gonçalves et al., 2016).

Previous studies have assessed the impact of SM at the mammary quarter level and reported a negative effect of mastitis on milk yield and composition, especially for specific groups of bacteria (Bezman et al., 2015; Forsbäck et al., 2009; Leitner et al., 2006). A recent study investigated a total of 650 lactating dairy cows selected from seven dairy farms to evaluate the effect of SM, caused by different microorganisms, on SCC, milk yield and composition, milk price, and economic performance (milk production × milk price), using the comparison of milk yield between contralateral mammary quarters (healthy x infected; Gonçalves et al., 2018a). The contralateral mammary quarters correspond to pairs of anterior or posterior mammary quarters since the contralateral mammary quarters produce a comparable amount of milk when healthy. Because these quarters have independent production of milk, this comparative approach would make it possible to assess production losses, changes in milk composition, and SCC of the healthy mammary quarter about the mammary quarter affected by the target pathogen under study. Thus, using milk sampling that allows comparison between contralateral quarters minimizes some factors that could reduce the study's accuracy, such as the effect of diet.

The study was carried out in two steps. Step 1 comprised collecting composite samples of milk when the cows had at least 2 of 3 weekly results of SCC >200,000 cells/mL (Dohoo & Leslie, 1991), and bacteriological cultures were positive (in the third sampling week), they were considered infected. A total of 146 infected cows were evaluated at the level of mammary quarters in the second step of sampling (15 days after the first step), with individual milk production at the quarter level being measured, followed by milk sampling for SCC, milk composition, and microbiological culture. Considering all results of microbiological culture of the mammary quarters (n = 584), 375 (64.2%) were culture-negative, whereas the most frequently isolated microorganisms were: a) *Corynebacterium* spp. (7.9%), b) *non-aureus* Staphylococci (5.8%), c) *Staphylococcus aureus* (5.3%), d) *Streptococcus uberis* (4.6%), e) *Streptococcus agalactiae* (3.9%), f) *Streptococcus bovis* (2.4%), g) Gram-negative bacteria (2.4%), h) *Enterococcus* spp. (1.4%) and i) *Streptococcus dysgalactiae* (0.68%; Gonçalves et al., 2018a). A total of 55 pairs of healthy contralateral quarters (control) were compared among them. No differences were identified in the fat content, milk yield, protein concentration, SCC, and economic performance. Otherwise, healthy mammary healthy mammary quarters (n=124 pairs) presented a lower geometric mean of SCC (153.60×103 cells/mL) than contralateral infected quarters (337.53×103 cells/mL). No effect of mastitis caused by minor pathogens on milk yield, SCC, and economic performance was observed. Contagious mastitis pathogens (i.e., *Streptococcus agalactiae* or *Staphylococcus aureus*) and environmental (environmental *Streptococcus* or Gram-negatives) SM-causing pathogens

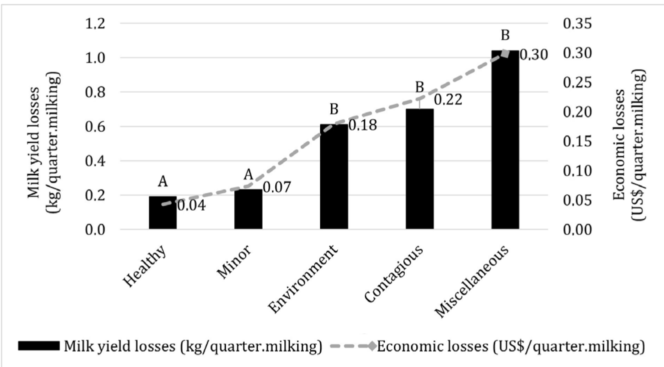

Figure 4 – Effect of SM according to the group of pathogens on milk yield and economic return (difference between 55 pairs of control healthy contralateral quarters and 124 pairs of healthy vs. infected contralateral quarters). Different letters represent differences in milk production between the groups of pathogens evaluated. Minor pathogens: *Non-aureus* Staphylococci and *Corynebacterium* spp. Environmental pathogens: environmental *Streptococcus* or Gram-negative. Contagious pathogens: *Staphylococcus aureus* or *Streptococcus agalactiae*. Infrequent pathogens: *Enterococcus* spp., *Nocardia* spp., Non-*aureus Staphylococci*, *Trueperella pyogenes*, and yeast. Adapted from Gonçalves et al. (2018a).

decreased milk production. They increased the SCC of infected quarters compared to contralateral healthy mammary quarters. Additionally, infected mammary quarters presented significant changes in the milk composition compared to healthy contralateral quarters. In summary, quarters infected by contagious pathogens decreased milk production by 0.7 Kg/milking. In comparison, quarters infected by environmental agents reduced milk production by 0.6 Kg/milking (Figure 4). Based on these estimated production losses and considering a prevalence of 9.2% of contagious and 10.1% of environmental mastitis pathogens which were diagnosed in the study, dairy herds would reduce US$ 712.8 of revenue/month associated with contagious mastitis [(−0.22 ×%contagious IMI quarters) × two milking/day] and US$ 637.2 per month for environmental mastitis [(−0.18 × %environmental IMI quarters) × two milking/day]. Every year, dairy farms were estimated to have a reduced economic performance of US$ 8,553.6 (for contagious mastitis) and US$ 7,646.4 (for environmental mastitis) whether the average of 10% per month was considered for IMI caused by both mastitis-causing pathogens during one year (Gonçalves et al., 2018a).

The ability of specific major pathogens to cause persistent infections (e.g., *Staphylococcus aureus*) can lead to the existence of chronic cases of SM and cause fibrosis of the secretory tissue of the mammary gland, irreversibly impairing the capacity of milk synthesis in the affected quarter (Benites et al., 2002; Botaro et al., 2015). Milk produced from mammary quarters with chronic mastitis caused by major pathogens has greater protein concentrations and ions Na+ and Cl-. These ions in milk are associated with altered permeability of the blood-milk barrier, which leads to the influx of whey proteins and concomitant outflow of lactose and K+ for blood circulation. Simultaneously, there is a lower content of fat and lactose, which may be associated with greater lipolytic enzyme activity in response to intramammary infection (Santos et al., 2003), and the decrease in milk production, as lactose is an important osmolarity regulating factor in milk synthesis (Forsbäck et al., 2010).

In another study, the impact of CSM on milk yield and composition was estimated using the approach of consecutive sampling of mammary quarters over time. The study was carried out in two steps. In the first step, SM and chronic (CSM) cases were identified among 647 lactating cows from six herds included in the experiment (Gonçalves et al., 2020). Cows were considered healthy when they had SCC <200,000 cells/mL and no microbiological isolation along the three consecutive samplings. SM was considered when microorganism was isolated and SCC >200,000 cells/mL in only one sample. CSM was considered when there was isolation of the same pathogen and SCC >200,000 cells/mL in at least two of the three samples performed. Udder quarters presenting CSM caused by major pathogens (e.g., *Staphylococcus aureus*; environmental *Streptococcus*) produced less milk (1.1 Kg/quarter/milking), fewer milk components and had higher SCC compared to healthy quarters (Gonçalves et al., 2020). On the other hand, when minor pathogens caused CSM (Non-aureus Staphylococci and *Corynebacterium* spp.), there was no loss in milk production, despite the increase in SCC in the affected quarter. These findings suggest that the impact of CSM on milk components and production depends on the type of the causative pathogen of the intramammary infection, with losses being greater in chronic cases and caused by major pathogens (Figure 5).

The increase in intramammary infections by minor pathogens is one of the main challenges for controlling SM in dairy herds (Haltia et al., 2006; Souto et al., 2008; Taponen & Pyörälä, 2009). For example, *Corynebacterium bovis* is a minor contagious pathogen for SM, and its isolation has been evaluated as an indicator of milking hygiene (Watts et al., 2000). The capacity and form of colonization of the mammary gland by *Corynebacterium* spp. are still controversial. Watts et al. (2000) described the ability only to colonize the teat canal. Nonetheless, *Corynebacterium bovis* can colonize the teat cistern, mammary gland, and parenchyma (Benites et al., 2003). There have been a growing number of studies on mastitis caused by *Non-aureus* Staphylococci (Pyörälä & Taponen, 2009). This group of pathogens is associated with a mild to moderate increase in SCC (Piepers et al., 2013). However, cases of intramammary infection by some species of the group (e.g., *Staphylococcus chromogenes*, *Staphylococcus simulans*, and *Staphylococcus xylosus*) may increase the SCC similarly to that observed in intramammary infections by

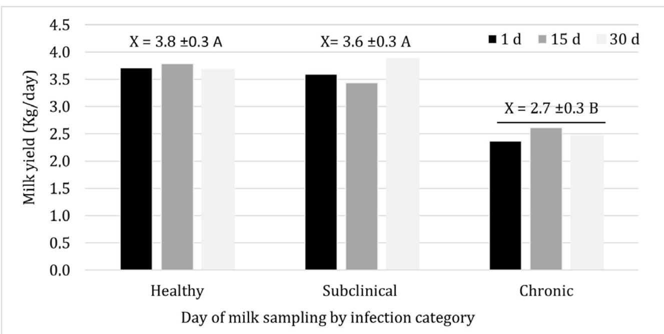

Figure 5 – Effect of subclinical and chronic mastitis caused by major pathogens on milk yield compared to healthy quarters. Different letters represent differences in milk production between categories. Adapted from Gonçalves et al. (2020).

Staphylococcus aureus (Supré et al., 2011). This is associated with some species' ability to adhere to mammary epithelial cells, some of which are equivalent to that of *Staphylococcus aureus* (Supré et al., 2011). In others, this ability is less accentuated (Pyörälä & Taponen, 2009). The ability to adhere to mammary cells influences the immune response to intramammary infection, which may explain the increase in SCC without reducing milk production (Supré et al., 2011). Additionally, greater adhesion capacity and potential damage to the secretory epithelium of the mammary gland are more present in species of *Non-aureus* Staphylococci adapted to the mammary gland.

Considering the particularities among the different microorganisms in the *non-aureus* Staphylococci group, its microbiological identification at the species level would be justifiable. The prevalence of SM caused by this group and the respective impacts on milk production and components have been the subject of studies because of the divergence of results. There were no effects of SM caused by *non-aureus* Staphylococci on milk composition and production, by the contralateral quarters' comparison, despite the increase in SCC in the mammary quarters infected by the *Non-aureus* Staphylococci group (Tomazi et al., 2015) or by the most frequent species, *Staphylococcus chromogenes*. Another study evaluated the effect of SM caused by *Corynebacterium bovis* on milk quality by comparing contralateral quarters (Gonçalves et al., 2016). Other species of *Corynebacterium* non-*bovis* are less prevalent and do not alter milk production and composition nor increase SCC compared to healthy contralateral mammary quarters. However, *Corynebacterium bovis* has a higher frequency of isolation and slightly altered SCC and lactose concentration without reducing milk production. The lowest lactose production was observed in quarters infected with *Corynebacterium* spp. which suggests that these agents colonize not only the teat canal, as lactose is produced in the mammary epithelial cells. Additionally, previous studies showed higher phosphorus content in mammary quarters infected by *Corynebacterium bovis* compared to healthy quarters (Coulona et al., 2002), which is indicative that intramammary infection by *Corynebacterium* spp. can act on the blood/milk barrier, changing the permeability of the mineral content.

Final Considerations

SM is a dominant form of mastitis in dairy herds and causes significant losses to the dairy industry. The main losses caused by SM are associated with the decrease in milk production and the milk quality bonuses. At the herd level, BTSCC was negatively associated with revenue, gross margin, and yearly profit per farm and cow. For each unit of increase in BTSCC, there was an average loss of 641 L cow/year (9.4%), considering a healthy cow when the SCC ≤200.000 cells/mL, with an average production of 6843.3 L. At the cow level, an increase in SCC from 100,000 to 270,000 cells/mL (for each increase of a log unit of SCC) resulted in losses of - 0.7 kg/day for first-lactation cows, -1.6 kg/day for second-lactation cows, and -2.3 kg/day for third-lactation cows. Healthy cows have higher milk yield when compared with chronically infected cows that were culture-positive caused by major pathogens (+7.1 kg/cow/day). The milk production loss associated with CSM was 44.9% for *Streptococcus* like-bacteria; 35.3% for *Streptococcus agalactiae*; 27% for *Streptococcus dysgalactiae*; 26% for *Streptococcus uberis*, and 24.5% for *Staphylococcus aureus*. At the mammary quarter level, no effect of mastitis caused by minor pathogens on milk production, SCC, and economic performance was observed when compared with contralateral healthy quarters. However, udder quarters infected by contagious mastitis pathogens had a reduced milk yield of 0.7 Kg/milking as well as environmental pathogens reduced milk yield by 0.6 Kg/milking compared to contralateral healthy quarters. Cows with mammary quarters with CSM caused by major pathogens (e.g., environmental *Streptococcus*, *Staphylococcus aureus*) produced even less milk (1.1 Kg/quarter/milking), fewer milk components, and presented higher SCC compared to healthy quarters. In summary, milk yield and composition losses varied with the milk sampling level, which is more accentuated in older cows with high SCC, and it is undoubtedly higher in chronic infection but depends on the group of mastitis-causing pathogens.

Conflict of Interest

The authors declare no conflicts of interest.

Ethics Statement

All the research conducted and detailed in this review manuscript received approval from the Ethics Committee on Animal Use of the School of Veterinary Medicine and Animal Science of University of São Paulo, with approval granted on June 26, 2013 (Approval number: 3020).

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