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Review on Epidemiology of Clinical and Subclinical Mastitis on Dairy Cows

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Summary
Mastitis is a complex and multi-factorial disease, the occurrence of which depends on variables related to the animal, environment and pathogen. It reduces the quality and quantity of milk, and is one of the most important and expensive disease of dairy industry. Among the pathogens, bacterial agent are the most common one, the greatest share of which resides widely distributed in the environment of dairy cows, hence a common threat to the mammary gland. Mastitis is very common in cows of both developed and developing countries. Based on clinical symptoms, it can be classified into two types, namely, clinical and subclinical mastitis. Clinical mastitis is often diagnosed directly by visual assessment of udder inflammation or by changes in milk's organoleptic properties whereas, Subclinical mastitis is non observable form of mastitis, which is with no visible abnormalities of either the milk or the udder and is characterized by sudden rise in milk somatic cell count. Mastitis pathogens can be divided into contagious and environmental. The primary reservoir of contagious pathogens is an infected udder whereas a contaminated environment is the primary reservoir of pathogens causing environmental mastitis. As in the rest part of the world, mastitis is one of the most economically important disease of dairy sector and is an important factor that limits dairy production in Ethiopia, giving emphasis only to clinical mastitis and subclinical mastitis, (with prevalence of 23% to 85%) is with little attention, causing heavy financial loses and public health hazards. Early diagnosis of mastitis is vital because changes in the udder tissue take place much earlier before they become apparent. Many factors influence the incidence of mastitis, such as Age, parity and lactation stage of a cow, lactation number, herd management, husbandry environment, temperature, humidity, seasons, breeds, and milking characteristics, and nature of the pathogen. If detected early, antibiotic therapy is very effective in curing and controlling the spread of contagious pathogens. However, The use of antimicrobials have, over time, increased the number of antimicrobial-resistant microbes globally, and any use of these agents will to some extent benefit the development of resistant strains and also inappropriate usage of antimicrobials such as wrong dose, drug or duration may contribute the most to the increase in antimicrobial resistance without improving the outcome of treatment.
Keywords: Mastitis, Ethiopia, dairy cows, antibiotic

1. Introduction

The production of meat and milk in the developing world has doubled in recent decades, as a result of increasing demands. This so-called "livestock revolution" provides; income, employment and high-quality nutrition, and the livestock are important to the food security of millions of people and the trend is expected to continue.[53] It has also been concluded that in great parts of the developing world, including developing countries of Africa, milk products consist a very important energy source for many people, and can contribute to a substantial part of the total energy intake.[11] However, infectious diseases, as mastitis, represent serious potential constraints to further development of smallholder production in developing countries and have been described as a factor that can drive rural smallholders into chronic poverty.[17]

Milk is one of the most important foods of human beings. It is universally recognized as a complete diet due to its essential components. However, mastitis reduces the quality and quantity of milk and is one of the most important and expensive disease of dairy industry.[2] It is a complex and multi-factorial disease, the occurrence of which depends on variables related to the animal, environment and pathogen.[31]Among the pathogens, bacterial agent are the most common one, the greatest share of which resides widely distributed in the environment of dairy cows, hence a common threat to the mammary gland.[12] The inflammatory response increases somatic cell count in milk. Somatic cells are very specific, and are only elevated in the mammary once infection occurred.[45] Besides health disorders of the mammary gland, mastitis can also cause significant losses in milk yield, alterations in its quality, fertility disorders and even systemic diseases.[21] Moreover, causative agents of mastitis with zoonotic potential may represent a health risk for human populations via the food chain. It results in severe economic losses from reduced milk production, treatment cost, increased labor, milk withheld following treatment and premature culling.[40] A wide range of pathogens including viruses, bacteria, fungi and their toxins can cause mastitis. Frequency of contagious pathogens among mastitis cases is greater.[37] The primary reservoir of contagious pathogens is the mammary gland itself. The infectious agent enters through the milk canal, interacts with the mammary tissue cells and multiplies.[51]The mammary tissue reacts to these toxins and becomes inflamed. The intra-mammary inflammatory response associated with mastitis results in a decrease in milk production and decrease in quality of milk and the manufactured products.[52] Besides increasing somatic cell count in milk, mastitis

results also in an increase of whey proteins, serum albumin, immunoglobulin, chloride, sodium, Ph, free fatty acids the milk.[29] Mastitis also results in a reduction in synthesis of the main components of milk, such as lactose, fat, non-fat solids and casein.[29] In general Bovine mastitis, the most significant disease of dairy herds, has huge effects on farm and country economics due to reduction in milk production (in quality and quantity), zoonotic effect and treatment costs.[37] Epidemiological investigation of bovine mastitis, status of infection, treatment pattern would provide useful management information to the producer, veterinarian and other mastitis control team members.[18] Therefore objectives of this review are to give a brief overview of the Prevalence of clinical and subclinical mastitis and to assess predisposing factors and control/prevention options.

2. Global epidemiology and risk factors of mastitis

2.1. Global epidemiology of mastitis

According to their epidemiology, mastitis pathogens can be divided into contagious and environmental. The primary reservoir of contagious pathogens is an infected udder whereas a contaminated environment is the primary reservoir of pathogens causing environmental mastitis.[11] *Streptococcus agalactiae*, *Staphylococcus aureus* subsp. *aureus* and *Mycoplasma* spp. are considered as typical contagious pathogens. Typical environmental pathogens are so-called environmental streptococci (streptococci other than *S. agalactiae* such as *Streptococcus uberis*; enterococci), *Enterobacteriaceae* and coagulase-negative staphylococci (CNS).[18] Over 140 different microorganisms have been isolated from bovine intra-mammary infection, but the majority of infections are caused by *Staphylococci*, *Streptococci* and *Enterobacteriacae*.[34]Bovine mastitis is mostly caused by *Streptococcus* species, like *S. agalactiae, S. dysagalactiae,* the leading organism is *Staphylococcus aureus,* producing acute suppurutive, gangrenus, or chronic mastitis depending on the infecting strains. Generally, Mastitis can appear in two forms i.e., clinical or overt and sub-clinical or hidden.[35] Sub-clinical mastitis is 15- 40 times more prevalent than clinical mastitis and causes high economic losses in most dairy herds.[2] There is a known relationship between particular pathogens and the form of the disease. For example, *S. uberis*, *Escherichia coli*, *Klebsiella* spp., *Pseudomonas aeruginosa* and pyogenic bacteria are mainly considered as causative agents of clinical mastitis.[18] On the other hand, *S. agalactiae*, CNS and *Enterococcus* spp. are associated with subclinical mastitis.[16] However, *S. aureus* has been designated as a causative agent of both clinical and subclinical mastitis.[2] The prevalence of bovine mastitis is higher in farms with larger herd sizes than in those with lower herd sizes.[35] The prevalence is also higher in cows with lesions and tick infestations on the skin, udders and teats than cows without these factors, in early lactation stage than in the mid-lactation stage.[14] Studies conducted in different countries of the world shows the prevalence range of 21.1% to 86.2% of subclinical Mastitis.[17&23]

2.2. Predisposing risk factors

Many factors influence the incidence of mastitis, such as production stages of a cow), lactation number, herd management, husbandry environment temperature, humidity, seasons, breeds, and milking characteristics.[3&4] Predisposing factors in the management and environment cause mastitis by negatively influencing the local and systemic barriers and defense of the cow, and/or by increasing exposure of the udder to micro-organisms in general they can be categorized into three.[53]

2.2.1. Environmental factors

Environmental conditions that can increase exposure include: overcrowding; poor ventilation; inadequate manure removal from the back of stalls, feeding areas and exercise lots; poorly maintained (hollowed out) free stalls; access to farm ponds or muddy exercise lots; dirty maternity stalls or calving areas; and general lack of farm cleanliness and sanitation.[12]

Bedding materials are a significant source of teat end exposure to environmental pathogens. The number of bacteria in bedding fluctuates depending on contamination (and therefore availability of nutrients), available moisture and temperature.[9] Low-moisture inorganic materials, such as sand or crushed limestone, are preferable to finely chopped organic materials. In general, drier bedding materials are associated with lower numbers of pathogens. Warmer environmental temperatures favor growth of pathogens; lower temperatures tend to reduce growth. [12]

2.2.2. Host factors (cow factors)

Age, parity and lactation stage found to be having significant difference on the prevalence of bovine mastitis. [53] Cows at age group of young adult and adult had an infection rate of 65% and 93.2%, respectively. Higher infection rate (87.2%) was recorded during the early lactation stage as compared to mid lactation stage that accounted for 65.9% and for late lactation (73.1%) also cows having greater than 5calves were more affected than those with fewer and moderate calves.[53] The infection rate of mastitis in cows with pendulous udder is higher than those with non pendulous udder the pendulous udder exposes the teat to injury, and pathogens may easily adhere to the teat and get access to the gland tissue. The infection rate in cows with teat lesions is more than cows with normal teats the prevalence of SCM is higher in high yielding cows than low to medium yielders. [43]

Rates of new intramammary infections caused by environmental streptococci and coli forms are greater

during the dry period than during lactation. During the dry period (i.e., the time between the last milking of one lactation and calving at the start of the next), the mammary gland undergoes a series of changes that influence the cow's resistance to bacterial infection.[4] Susceptibility to intramammary infection is greatest the two weeks after drying off and the two weeks prior to calving. Many infections acquired during the dry period persist to lactation and become clinical cases. Research has shown that 65% of coliform clinical cases that occur in the first two months of lactation are from intramammary infections that originated during the dry period. Streptococcal infections during the dry period account for 56% of clinical cases during the first two months after calving.[9] Therefore, the thrust of herd management strategies for controlling environmental mastitis should focus on reducing intramammary infections during the dry period and early lactation.[12]

2.2.3. Agent/pathogen factors

Bacteria require virulence factors to colonize, multiply and survive in the udder.[21] These include toxins, adhesions, invasions, capsule production and the ability to resist serum complement.[21] Virulence factors may be divided in three functional categories: Factors that mediate adhesion of bacteria to host cells; those that produce tissue damage; and those that protect the bacteria against the host's immune system and antibiotics.[15]

3. Prevalence of mastitis in Ethiopia

Mastitis, as a disease, has received little attention in Ethiopia, especially the subclinical form which is mainly caused by Staphylococcus *aureus*.[13] Efforts have only been concentrated on the treatment of clinical cases. Owing to the heavy financial implications involved and the inevitable existence of latent infection, it is obviously an important factor that limits dairy production. The disease should be studied as it causes financial losses as a result of reduced milk yield and quality, discarded milk following antibiotic therapy, veterinary expense and culling mastitic cow.[13] Several studies conducted in different corners of the country indicated a prevalence range: (13.7% to 81.1%) over all prevalence of mastitis.[43&5] (23% to 85%)[43& 52] prevalence of subclinical mastitis, (2.6% to 62.9%)[24&4] of clinical mastitis and (12.3% to 80.88%)[24&5] prevalence at a quarter level in small and large scale dairy farms. In general, mastitis is of great economic importance to all dairy producers and also in pastoral and agro-pastoral dairy production systems of the country.[3]

4. Types of mastitis

4.1. According to mode of transmission of pathogen

4.1.1. Contagious mastitis

Among infectious agents, bacterial pathogens are major threat to mammary gland. These microorganisms are often contagious, widely distributed in the environment of dairy animals and thus increase prevalence rate of intra-mammary infections.[40] The sources of contagious mastitis are infected cows and transmission is from cow to cow, mainly at milking time through milking equipment, the milker's hands and contaminated wash cloths. The principal contagious pathogens are *Streptococcus agalactiae*, *Staphylococcus aureus, Corynebacterium bovis* and *Mycoplasma* species. Among these, *S.aureus*, is currently the most frequently isolated contagious pathogen in subclinical and chronic bovine mastitis worldwide.[51]These bacteria can be controlled effectively by procedures that prevent spread of bacteria at milking time including good udder hygiene, proper milking procedures, and post milking teat disinfection. Use of dry cow therapy can help eliminate existing infections and prevent new infections during the early dry period.

4.1.2. Environmental mastitis

Environmental mastitis is caused by organisms that do not normally live on the surface of the skin or in the udder, but which enter the teat canal when the cow comes into contact with a contaminated environment.[12] The primary source of environmental pathogens is the surroundings in which a cow lives.[6]Those pathogens causing environmental mastitis (Str. *uberis*, Str.*dysvcagalactiae*, coliforms, etc.) present in the environment (bedding, flooring, droppings) generally transmitted in any time of cow's life: during milking, between milking, during the dry period, especially at first calving, in heifers.[34]

Housed cows are at greater risk for environmental mastitis than cows on pasture. Bedding is a major source of environmental pathogens. The number of infectious bacteria in bedding depends on its temperature, moisture level and nutrient availability. Infections with environmental Streptococci, Klebsiella, and Enterobacter occur more frequently early in the dry period. On the other hand, E. coli infections tend to occur immediately before and after calving. It is thus very important for both far-off and close-up dry cows to be kept in lots with dry clean bedding to minimize the risk of new infections.[12]

4.2. According to the clinical symptoms

4.2.1. Clinical mastitis

On the farm, mastitis is usually detected by the observance of abnormal milk such as flakes, clots, or a watery appearance. The udder producing this milk may become swollen, red, hot, and hard and there may be also fever, rapid heart rate and loss of appetite.[23] This condition is known as clinical mastitis and is observed in less than 5%

of animals in a well-managed dairy herd.[46] Cows that developed clinical mastitis suffered an immediate drop in production and will not regain previous production levels during the 60 days following the clinical onset.[13]

Clinical mastitis is defined as the production of abnormal milk with or without secondary symptoms such as swollen quarters, elevated body temperature and/or other systemic signs.[22] Although clinical infections are rarely apparent prior to calving, routine observation for abnormal swelling is important. Normal prepartum udder secretions range from a honey-like appearance to normal milk.[20] Clinical mastitis can be recognized in pre- and post-calving secretions, colostrum or milk by the presence of gargot (clots and flakes), abnormal texture or discoloration.[48]

4.2.2. Sub clinical mastitis

The non observable form of mastitis, such as no visible abnormalities of either the milk or the udder, is known as subclinical mastitis.[16] In excess of 50% of animals in a herd can have subclinical mastitis at any given time.[46] A sudden rise in milk somatic cell count observed in normal milk from normal udders may indicate the presence of subclinical mastitis. Animals which have subclinical mastitis are usually not producing milk to their full potential and can serve as a potential source of infection to healthy udders.[46]

The subclinical form of mastitis in dairy cows is important because this form is (a) 15 to 40 times more prevalent than the clinical form, (b) it usually precedes the clinical form, (c) it is of long duration, (d) it is difficult to detect, (e) It reduces milk production, and (f) it adversely affects milk quality g) constitutes a reservoir of microorganisms that can affect other animals within the herd due to its contagious nature.[32] Besides causing huge losses to milk production, the sub clinically affected animals remain a continuous source of infection to other herd mates. If the infection persists for longer periods, then it may form a fibrous tissue barrier between the organisms and the antibiotic preparations, thus, limiting their efficacy.[16]

5. Diagnostic techniques

Monitoring udder health performance is impossible without reliable and affordable diagnostic methods. The diagnosis of mastitis according to the International Dairy Federation (IDF) recommendations is based on the SCC and microbiological status of the quarter.[40] It is essential to diagnose mastitis at the initial stage of infection to initiate the treatment as early as possible before the bacteria is anchored in the mammary gland.[19] Early diagnosis of mastitis is vital because changes in the udder tissue take place much earlier before they become apparent. Various methods, based on physical and chemical changes of milk and isolation of organisms, are used for diagnosis of subclinical mastitis.[8]

5.1. Clinical diagnosis

Mastitis may lead to clinical symptoms and, as a consequence, it is often diagnosed directly by visual assessment of udder inflammation or by changes in milk's organoleptic properties.[33] Milk from healthy, uninfected mammary glands has a white to white-yellow appearance and is free of flakes, clots, or other gross alterations in appearance. Such abnormalities are indicators of milk that is unsuitable for human consumption. The presence of flakes, clots, or other gross alterations in appearance of quarter milk is evidence of clinical mastitis and is by definition, abnormal milk.[29&20] Clinical syndromes are based upon the severity of the inflammatory response. Symptoms include redness, swelling, heat, pain, and loss of function including decreased production, change in composition, and change in appearance. The clinical syndromes include per acute, acute, sub acute, and chronic.[20]

5.1.1. Peracute mastitis: is characterized by a sudden onset, severe inflammation of the udder, serous milk and systemic illness. The systemic illness is due to septicemia or toxemia, results in fever, anorexia, depression, decreased rumen motility, dehydration, and sometimes death of the cow. Systemic illness often precedes the symptoms manifested in the milk and mammary gland.[20]

5.1.2. Acute mastitis: Acute mastitis is characterized by a sudden onset, moderate to severe inflammation of udder, decreased production, and serous milk/fibrin clots. Systemic signs are similar but less severe than the per acute form.[20]

5.1.3. Sub acute Mastitis: Sub acute mastitis is characterized by mild inflammation, there may be no visible changes in udder, there are generally small flakes or clots in the milk, and the milk may have an off-color. There are no systemic signs of illness.[20]

5.1.4. Chronic Mastitis: Chronic mastitis may persist in subclinical form for months or years with occasional clinical flare-ups. Treatment usually involves treating the clinical flare-ups, or culling the cow from the herd.[20]

5.2. Somatic cell count

Somatic cell counts (SCC) in milk are commonly used as indicators of mastitis, on the basis that an increase reflects an immune response to the presence of infection in the mammary gland.[8] An infection is assumed when a specific concentration (normally 100,000 cells/ml of milk) is exceeded while bacterial infection can cause it to increase to above 100,000 cells/ ml. A cell count of 200,000 cells/ml or greater is a clear indication that an inflammatory response has been elicited (subclinical mastitis), the quarter is likely to be infected.[6]

Somatic cells are mainly milk-secreting epithelial cells that have been shed from the lining of the gland and white blood cells (leukocytes) that have entered the mammary gland in response to injury or infection. Somatic cells found in milk are mainly leukocytes, whose principal function is to eradicate infections, and repair damaged tissues.[45] Somatic cells are indicators of both resistance and susceptibility of cows to mastitis and can be used to monitor the level or occurrence of subclinical mastitis in herds or individual cows. SCC is a useful predictor of intra- mammary infection (IMI), and therefore, an important component of milk in assessment of aspects of quality, hygiene and mastitis control[8&29]. The contagious pathogens (*Staphylococcus aureus*, *Streptococcus agalactiae*) generally cause the greatest SCC increase. An infection by environmental pathogens (*Strep.dysagalactiae*, *Strep.uberis*, *Corynebacterium bovis* and Coagulase negative Staphylococcus) usually causes considerably less SCC elevation.[35] Somatic cell counts are widely used to predict the mammary health status of quarters and cows the suitability of milk for human consumption and monetary losses to producers due to mastitis.[12]

5.3. California mastitis test (CMT)

The CMT is a cow-side test, so the results are available immediately (milk sample does not have to be sent to a laboratory to obtain the somatic cell count value). For 50 years the CMT has been the only reliable cow-side screening test for subclinical mastitis. Although it does not identify the type of bacteria that cause mastitis, the CMT is useful in identifying quarters that have high SCC. The degree of reaction between a reagent and the DNA of cell nuclei indicates the number of somatic cells in a milk sample, however, the relationship between SCC values and CMT is not precise because of the high degree of variability in SCC values within each CMT score.[48] The test is very simple, can be performed at milking time, gives instant results and is economical. It will be carried out as screening test for sub-clinical mastitis and for selection of samples for culture. A squirt of milk, about 2 ml from each quarter will be placed in each of four shallow cups in the CMT paddle. An equal amount of commercial reagent will be added to each cup. A gentle circular motion will be applied to the mixtures, in horizontal plane for 5s. The reaction will be interpreted based on the thickness of the gel formed by CMT reagent and milk mixture, and the test result will be scored as negative (0), trace (T), + (weak positive), ++ (distinctive positive) and +++ (strong positive) according to.[36]Quarters with CMT score of (+) or above will be judged as positive. Cows will be considered positive when at least one of the quarters becomes positive for CMT and a herd will be considered positive, when at least one cow in the herd tested positive with CMT. The CMT gives an indirect estimate of SCC because it based upon a gelling reaction between the nucleic acid of the cells and a detergent reagent. The CMT is first choice of diagnosis in several investigations because it is more perfect, efficient and reliable than other field and chemical tests for diagnosis of subclinical mastitis.[34]

5.4. Surf field mastitis test

The principle of the test is that when detergent is added into milk sample, it causes rupture of somatic cell and release DNA and other cell contents. DNA is acid in nature, while detergent contains alkyl-arylsulfonate, which is basic in nature. DNA and detergents unite to form a gel; consistency of gel depends upon the number of somatic cells.[33] More cells, more thick gel and vice versa**.** Quarter milk samples and surf solution mixed in equal quantities in petri-dishes separately for each quarter. The change in consistency of milk indicates mastitis, while no change in consistency of milk indicates healthy samples. The mastitis (the reaction of the mixture) will be graded into further four categories based on the severity of disease from lower to higher intensity as, + = moderate, ++ = severe, +++ = more severe, ++++= very severe.[36]

5.5. Bacteriological examination

Bacteriological culturing can be executed at herd, as well as cow and quarter level, each with its own specific goal. Bacteriological culturing is most often used as a diagnostic tool to solve mastitis problems. Knowledge on the infectious status of mammary glands, however, can also be very helpful to prevent transmission of pathogens by diagnosing a reservoir at an early stage. To effectively use bacteriological culturing as a diagnostic tool, milk samples have to be collected from the correct cows and quarters at the correct point in time.[19] Proper collection of milk samples is of paramount importance for identification of mastitis pathogens. Aseptic technique is an absolute necessity when collecting milk samples to prevent contamination by organisms found on the cows' skin, udder, and teats; hands of the sampler; and in the barn environment. Contaminated samples result in misdiagnosis, increased work and expense, confusion, and frustration.[29]

6. Public health importance

The bacterial contamination of milk from affected cows render it unfit for human consumption and provide a mechanism of spread of diseases like tuberculosis, sore-throat, Q-fever, brucellosis, leptospirosis etc. and has zoonotic importance.[40] Milk and other dairy products are frequently infected with *S. aureus.* Milk of infected animals is the main source of enterotoxigenic *S. aureus* of animal origin. For example certain *S. aureus* strains produce heat-resistant enterotoxin, which cause nausea, vomiting and abdominal cramps when ingested by humans

and are responsible for staphylococcal food poisoning outbreaks.[18]

Another public health concern regarding mastitis is antibiotic residues in milk due to extensive use of antibiotics in the treatment and control of the disease.[49] Antibiotic residues in foods can lead to severe reactions in people allergic to antibiotics and, at low levels, can cause sensitization of normal individuals and development of antibiotic-resistant strains of bacteria.[18]

7. Economic impact of mastitis

Mastitis remains the most common and the ambiguity disease of dairy cattle throughout most of the world. It continues to be the most economically important disease of dairy industry, accounting for about 38% of the total direct losses.[37] It is the most economically important disease in the dairy industry in USA, estimated losses ranging from $185.00 to 265.00 per cow per year. This places annual losses in excess of $2 billion or about a 10% loss of total productive capacity. Generally, sources of economic loss include reduced milk production, animal replacement due to culling, discarded milk due to antibiotic treatment, cost of treatment, veterinary service, and extra labor cost to care for the animals.[46&40]

Mastitis affects the milk quality in terms of decrease in protein, fat, milk, sugar (lactose) contents and increase in somatic cell count. The processing of such milk results in substandard and sub-optimal output of finished fermented products like yogurt, cheese etc.[40]Mastitis had been known to cause a great deal of loss or reduction of productivity, to influence the quality and quantity of milk yield, and to cause culling of animals at an unacceptable age. Most estimates have shown a 30% reduction in productivity per affected quarter and a 15% reduction in production per cow per lactation.[34] It has adverse effects on the economics of milk production by reducing the quantity (approx. 21%) and quality (butter fat 25%) of milk.[35] Losses due to mastitis may even be higher in developing countries because standard mastitis control and prevention practices (e.g. pre and post milking antiseptic teat dipping and dry period antibiotic therapy) recommended by National Mastitis Council (NMC) of USA are not being carried out in these countries.[48]

8. Harmful effects beyond udder on dairy cows

Several studies indicated that both clinical and sub-clinical mastitis alter the reproductive process at several levels.[28] Mastitis delays the postpartum ovarian function and alters some of the key reproductive functions like ovulation, fertilization, implantation, and pregnancy maintenance.[29] Acute mastitis delays the calving to first service interval, calving to conception interval and increase the number of services per conception. When clinical mastitis occurs before the first artificial insemination (AI), calving to first service interval is significantly increased, compared to when it occurs after the first AI.[10] It has been reported that the probability of conception decreased by 44 per cent when mastitis occurred a week before insemination, by 73 per cent when it occurred during the week of insemination, and by 52 per cent when mastitis occurred during the week after insemination. Bacterial toxins released during mastitis influence conception and early embryonic survival in affected cattle by stimulating the production of prostaglandin F2α, which subsequently causes luteal regression, thus potentially causing the loss of an established pregnancy.

The effect of mastitis is not only limited to the affected animals but also continues to the developing fetus, since the daughters born to the cows that suffered mastitis during gestation had reduced reproductive efficiency. Anti-Mullerian hormone, a reliable biomarker for potential fertility, is severely decreased in the developing fetus as the number of mastitis events during gestation of their dams increases.[28]

9. Treatment of mastitis

The success of bovine mastitis therapy depends on the aetiology, clinical presentation, and antimicrobial susceptibility of the aetiological agent among other factors.[26] Therapy failure in the management of mastitis could result from pathological changes that occur in the udder, aetiology related factors, pharmacokinetic properties of the antimicrobial drugs, poor animal husbandry and inadequate veterinary services. An important question regarding the treatment of mastitis is whether the antimicrobial should accumulate in the milk or in the udder tissue.[7] The target site may depend on the causative agent: streptococci are known to remain in the milk compartment, but S. *aureus* penetrates udder tissue and causes deep infection. The most common route of administration of antimicrobials in mastitis is the IMM route. Systemic treatment is recommended in clinical mastitis due to S. *aureus* and in severe cases of coliform mastitis, preferably in combination with IMM treatment.[11] The systemic route of administration has been suggested to be more efficient than IMM for the treatment of clinical mastitis as antimicrobials theoretically have better penetration of the udder tissue by this route.[7] Antibiotic therapy is usually prescribed when clinical symptoms of mastitis are presented. If detected early, antibiotic therapy is very effective in curing and controlling the spread of contagious pathogens. However, antibiotic therapy is not effective against environmental pathogens, especially coliform bacteria. Culling is another method of control especially when dealing with chronically infected animals. This eliminates the potential source of infection at the expense of purchasing a replacement animal.[46]

9.1. Development of antimicrobial resistance

The use of antimicrobials have, over time, increased the number of antimicrobial-resistant microbes globally, and any use of these agents will to some extent benefit the development of resistant strains and also inappropriate usage of antimicrobials such as wrong dose, drug or duration may contribute the most to the increase in antimicrobial resistance without improving the outcome of treatment.[50] The increase in resistance to antibacterial agents has raised serious concerns worldwide from both public health and food safety perspectives, putting their use in food-producing animals under constant scrutiny over the years.[49]

9.2. Antibiogram susceptibility test

Identification of mastitis pathogens and their antimicrobial susceptibility is important when selecting appropriate treatment regimen.[36] Antibiogram studies of mastitis pathogens are also important to provide quality milk to the consumers and to prevent antibiotic resistance, potential health risk for humans.[31]The antibiogram profile of different bacterial isolates indicated that enrofloxacin, norfloxacin, ciprofloxacin and gentamycin proved to be the most effective antimicrobials against mastitis causing bacteria in different studies.[14&44] In these studies, Penicillin was found to be least effective antibiotic against bacterial isolates. This may be due to indiscriminate and frequent use of this antibiotic in dairy animals leading to development of antibiotic resistance.[14]

10. Prevention and control

Bovine mastitis is an endemic disease that cannot be completely eradicated. The wide ranges of microorganisms that can cause this disease, and the ubiquity of these organisms, make complete eradication unlikely.[40] Optimum control therefore lies in first understanding the epidemiology of the disease and the causal agents and then implementing an integrated control strategy.[51]

The control of mastitis has been successfully achieved through the establishment of effective herd health control programs.[7] Early diagnosis of mastitis with reliable tests facilitates successful treatment and control. The main control principles include: sound husbandry practices and sanitation, post milking teat dip, treatment of mastitis during non-lactating period, and culling of chronically infected animals.[40] Successful control of contagious mastitis pathogens is focused on reducing exposure of teats to pathogens found in milk that originated from infected cows. Control of environmental mastitis can be achieved by reducing the number of bacteria to which teat is exposed, increasing immune resistance of the cow, pre milking teat dipping with a germicidal.[28] Animal environment should be as clean and dry as possible. Antimicrobials are routinely used for treatment of dairy cattle affected with clinical and subclinical infections.[1]

The teat canal remains open up to 2-3 hours after milking to resume its normal confirmation. This is the reason for providing feed and water immediately after milking to encourage animals to remain standing and the reason for having freshly cleaned and bedded stalls when the cows do lie down.[40] As the weaning is not practiced by most of dairy farmers and direct calf suckling is practiced from the dam udder, the calf during feeding often damages the udder and infection develops. During suckling the pathogens may get entry into the teat. Calf suckling must be avoided at all costs in dairy animals.[39] Proper ventilation and good sanitation at the farm building is necessary to decrease the exposure of pathogens to the mammary gland.[31] The milker's hand should be properly washed, dried and cleaned so that chances of spread of disease can be minimized. All milking utensils should also be clean and dry. Dry bedding should be provided. The dung and urine should be removed immediately, as these are constant source of infections at the farm.[40] Recently, the National Mastitis Council of USA and Canada expanded the five-point plan to a ten-point plan with 73 sub-points. The ten points are: (a) establishment of goals for udder health; (b) maintenance of a clean, dry and comfortable environment; (c) proper milking procedures; (d) proper maintenance and use of milking equipment; (e) good record keeping; (f) appropriate management of clinical mastitis during lactation; (g) effective dry cow management; (h) maintenance of bio-security for contagious pathogens and culling of incurable and chronically infected cows; (i) regular monitoring of udder health status; and (j) periodic review of the mastitis control program.[28] Dry cow treatment, milking technique, post-milking teat dipping and antimicrobial treatment of clinical mastitis are examples of management factors that have a significant effect on the reduction of mastitis cases and bulk tank milk SCC.[21] Although subclinical mastitis is the dominant form affecting cows, it frequently goes undetected or untreated for extended periods by most dairy producers, chronic subclinical infections have long been recognized as a major barrier in the control of mastitis on dairy farms.[11]

Other general practices to prevent contagious and environmental mastitis include the milking of infected animals last and preventing the animals from lying down after milking. This can be accomplished by feeding them immediately after milking to insure that they are standing for at least 30 minutes. This should allow enough time for the proper closure of the teat orifice.[46] whereas under Ethiopian conditions most of households use hand milking and washing hands, udder and teats before milking is not practiced, this could predispose Dairy cows for Pathogens.[3]

11. Conclusions and recommendations

This review revealed that Mastitis is the major problem of dairy farms both in developed and developing nations and the subclinical form is the most prevalent when compared to clinical mastitis. Worldwide, a lot of effort has been focused on how to minimize the effects of subclinical, clinical and recurrent (chronic) mastitis. Despite all these efforts the causative agents are ahead of us. To win the battle against Mastitogenic bacteria, it is essential that all infected cows are rapidly detected and isolated from other animals and that proper milking management and other preventive measures are used to minimize the spread of bacteria. Culling of old and chronically affected cows, screening of cows and milk for clinical and subclinical mastitis, dry cow therapy, hygiene at milking and husbandry system should be considered in attempts to reduce prevalence of mastitis. Moreover, extension services and training programs aiming at creation of awareness about the importance and prevention of subclinical mastitis among smallholder dairy farmers, milking infected animals and their respective quarters at last and periodic monitoring of infection status of the udder is recommended. Good management might help in the reduction of prevalence of subclinical mastitis. For early detection of subclinical mastitis CMT can be performed on a regular basis as a control measure. By identifying the causal agent, the best antibiotic could be used to counter a specific bacterium species.

12. References

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