



## Effect of Mastitis on Behavioral Changes of Dairy Cows, its Treatment and Control

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### Abstract

Livestock sector play an important role in the economy of Pakistan as well as it is a livelihood of farmer. These reared these animals to meet the consumption of milk, meat and other products. Mastitis comes among the one of the common and high paying problem of the dairy industry. It is ranked as a number one pathological condition of dairy farm animal. It effect the both corporate and commercial dairy farm. It contribute a major economic loss in farm income both at small level that is commercial farm as well as at large scale industries like corporates farms. The purpose of this review article is to indicate the major causes of mastitis like clinical as well as subclinical mastitis, its behavioral changes observed in animal, treatment protocol applied and drug of choice used at farm to control the mastitis. We will also point out that why sub-clinical mastitis is more important and what are the major changes that occur in mastitis milk with respect to the mastitis free milk. In this review article we will also discuss the bacteria that are involved in causing mastitis. We will also put a light on pathogenesis of mastitis as well as predisposing and other factor that are helpful in causing mastitis in this article. By this study we will estimate that which method or treatment plan is good for the treatment of mastitis and how we can prevent the occurrence of mastitis. In this review article will also know that what is clinical mastitis, what is subclinical mastitis and what are behavioral changes and treatment protocol that can be used to prevent and control mastitis. We will also gave a quick review to the total losses that are caused by mastitis. For the identification of mastitis, the changes that comes in the behavior of animal is of very important. Mastitis is still one of the major issue of dairy farm that increase the cost of production of milk and if we control it, it will be major achievement in dairy industry.

**Keywords:** Mastitis; Types of Mastitis; Behavioral Changes; ; Genetics and Nutrition Role; Bacteria; Treatment

### Introduction

In Pakistan, livestock sector play an important role in the economy [25] as well as livelihood of farmer in the form of different dairy animal like cattle, sheep camel, goat and buffalo [2,15,14]. These animal are reared basically to meet the consumption of milk, meat and other products in tropical and subtropical area of Pakistan [36,2]. A major population of Pakistan involve in rearing cattle (33.0 million) and buffaloes (29.9 million) sharing more than 95% of the total milk production of the Pakistan [8]. In Pakistan in arid and semi-arid region, cattle, buffaloes and camel are considered as the important milk producing animals [30]. However different viral [15], bacterial [24] fugal and parasitic agent cause different problem in dairy sector [3,6]. Among bovines, the

animal that are more susceptible to mastitis is cattle as compare to buffaloes and it is reported in many of the researches as well [33]. These problems become constraint in dairy sector affecting both productivity as well as food security for human consumption [38]. Among these problems, Mastitis is one of the most common and costly problem of dairy animals. It is reported that mastitis is one of the biggest and 1st problem of dairy industries as well as in field that veterinarian face in Pakistan [23]. On an average In Nili-Ravi buffaloes, mastitis decrease lactation period of each animal by 57 days and reduces 438 kg of milk per lactation [4]. It is also reported that about 240 million per year loss is due to mastitis [5]. Milk disposal, cost of treatment, culling of animal, low milk production and ultimately replacement of animal are the reason of losses that oc-

cur due to mastitis, We can detect clinical mastitis by examination of milk but sub clinical mastitis cause major loses in dairy farm as it is difficult to diagnose and can only be diagnosis by California mastitis test or more precisely somatic cell count (SCC) of the milk. Subclinical mastitis is more prevalent (15 to 40 times) then clinical mastitis. Similarly Sub- clinical mastitis is also have a long duration as it is less detectable and act as reservoirs of pathogen.

**Pathogenesis**

Mastitis is a disease that is caused by multiple factor in milk producing animal. Early diagnosis of mastitis and understanding of its pathogenesis is a very important [22]. After milking or post milking teat opening as well as teat canal of animal remain open and pathogen enter from teat opening to teat canal and ultimately to mammary gland cause mastitis [29]. A researcher in his resent research reported that a high number of bacterial population *strep-tococci* and *staphylococci* are already present on the teat skin and become cause of mammary gland infection [10]. Mammary gland parenchyma provide and optimum condition and temperature for the growth of bacteria [26]. Externally teat canal is covered by a layer of smooth muscle that help them to closed the teat canal and prevent the entry of pathogen [10]. Derived from stratified squamous epithelium, Teat canal is also covered with the layer of keratin from inside which protect the teat canal from inside. If this keratin layer is effected it is reported that the chances of mastitis are increased as it become opportunistic to the entry and colonization of bacteria [37]. Accumulation of fluid occur within the mammary glands when animal comes near to parturition which lead to increase in intra-mammary pressure as a result teat canal is dilated and leakage of mammary gland secretion occur which in result increased the vulnerability of mammary gland to infection [27]. At the time of milking, teat canal opened and bacteria enter from teat canal and damage to keratin layer of teat canal and lead to mastitis [17]. It is also reported that, after milking the teat canal remain partially open for 1-2 hour and in this time the mastitis causing agent are more prone to enter into the teat canal and damage to mammary gland [10]. As bacteria invade from teat canal, they circumnavigate the cellular and humoral defense mechanism of the body [10]. The form biofilm which cause the proliferation of bacteria and as a result bacteria release toxin and cause induction of leukocyte and epithelial cell to release cytokines, TNF Alfa, interlukin-8, IL-1, eicosanoids like PGF2 Alpha, radicals, and acute phase protein (APPs) [10]. Immune system work and causes the release of oxidants, protease that destroy bacteria and in result milk production is decreased and release of different enzyme like lactate dehydrogenase and N-acetyl-b-D-glucosaminidase occur. Dead and sloughed off epithelial, mammary cell and leucocyte comes in ilk and in result somatic cell count of milk is increased [10]. As the infection persist, swelling of mammary gland occur, alveoli become damaged, extracellular components like sodium, hydrogen, potassium and chloride enter into the gland and result in breaking

the blood-milk barriers which result in change the normal value pH, conductivity and milk taste [40]. Mastitis can be categorized into acute, chronic, gangrenous, mycotic and different sub clinical forms. Mastitis is characterized by inflammatory response [39]. The severity of inflammatory response is dependent upon both the host (parity, the stage of lactation, age, immune status of the animal and somatic cell count) and pathogen factors (species, virulence, strain and the size of inoculum of bacteria) [11,12]. In result of inflammatory response and infection release of different harmful toxin occur that ultimately result in increase in somatic cell count and tissue changes [17,11]. Neutrophil, lymphocyte, macrophages and minute or less number of epithelial cell constitute the somatic cell of milk [1,11]. Severity of infection vary from no visible or sub clinical mastitis to clinical mastitis causing systemic signs and ultimately leading to toxic mastitis and udder fibrosis [11].

Sr. no	Score	Description
	Mild	Abnormal milk (e.g., clots, flakes and watery)
	Moderate	Abnormal milk and signs of udder inflammation (e.g., heat, swelling and pain)
	Severe	Systemic illness (e.g., fever, dehydration, weakness and in-appetence)

**Table 1:** Severity scoring system for mastitis.

Source of this table [31].

**Impact of mastitis on cow behavior**

As we all know the first thing which owner notices is behavioral change in the animal. Animals’ pain threshold and physiological and behavioral responses to different pathological conditions and pain can vary depending on how severely it effecting animals’ physiological and behavioral functioning [21]. Invading pathogens initiate energy-demanding processes in the body, functioning to increase the effectiveness of the immune system to overcome the infection, e g, by increasing body temperature [19]. Then energy will be switched from behavioral activities, such as feeding, social contact, or grooming [19], and ill animals might have a different set of behavioral priorities, leading to changes in the social and environmental needs of the individuals. So, we can say knowledge of sickness behavior is an important foundation for future design of housing systems for sick dairy cows. Previous studies of sickness behavior in dairy cows, during either naturally occurring or experimentally induced mastitis, have presented relatively small data sets and mainly focused on crude behavioral changes, showing that mastitis can lead to reduced rumination, reduced feeding time and intake, as well as changes in resting behavior [34]. Cows showed classic signs of sickness behavior [34]. on the day they were diagnosed with clinical mastitis, displaying the least feeding and competitive behaviors. These behaviors have been also reported in studies with experimentally induced clinical mastitis [34]. Another researcher in his research reported that there is more risk of in-

crease somatic cell count in with udder injures and feeding animal with high concentrate diet [35].

**Mastitis causing bacteria**

The causative organisms of mastitis in buffaloes have been reported to be most probable are Staphylococci, Streptococci, Escherichia coli, Pseudomonas spp., Corynebacterium, Mycoplasma, Streptococcus dysgalactiae, and Mycobacterium tuberculosis [23]. In Pakistan, etiological agents of mastitis in buffaloes have been reported to be mostly Staphylococcus aureus, Staphylococcus hyicus, Staphylococcus epidermidis, Staphylococcus capotus, Streptococcus dysgalactiae, Streptococcus agalactiae, Streptococcus pyogenes and Corynebacterium bovis [23].

**Effect on Milk Composition**

Constituent	Normal milk	Mastitis milk with high SSC
Fat	3.5	3.2
Lactose	4.9	4.4
Total protein	3.61	3.56
Total casein	2.8	2.3
Whey protein	0.8	1.3
Serum albumin	0.02	0.07
Actoferin	0.02	0.1
Immunoglobulin	0.1	0.60
Sodium	0.057	0.105
Chloride	0.091	0.147
Source: [20].		

**Table 2**

**Effect of nutrition on Mastitis**

Nutrition plays an important role in controlling mastitis directly and indirectly by enhancing the immune system [41]. A balanced diet in total mixed ration of dairy cows, especially in high milk-producing herds, is most important to control mastitis [42]. The Total Mixed Ration or complete ration help the cow to combat pathogens to decrease the chance of mastitis by acting as an antioxidant by boosting the immune system of the animal [41]. Secondly, a complete diet will reduce the metabolic problems and negative energy balance that directly help stronger immunity and decrease the chances of mastitis [41]. A researcher in his research indicated that a cow supplemented with negative DCAD before parturition can help increase the metabolism of calcium and decrease problems that occur after parturition and indirectly would be helpful in controlling mastitis [43].

**Importance of micronutrients**

Micronutrients	Important in;	Micronutrients	Important in;
Vit. A	Decrease fatty acid Peroxidation	Copper	Peroxyl Scavenger
Selenium	Decrease ROS	Copper + Zinc	Cystol superoxide to hydrogen peroxide conversion
Manganese	Mitochondrial Superoxide to H2O2 Conversion	Iron	H2O2 to water conversion
Vit. C and Zinc	Radical Scavenger	[44]	

**Table 3**

These minerals and micro minerals play an essential role in animal immunity, keratin formation, reducing somatic cell count, and preventing prepartum and postpartum metabolic problems that decrease the incidence rate of mastitis in both high and low milk-producing herds [41].

**Role of genetics and nutrition**

Animal resistance to mastitis and role of genetics are an important point discussed in many papers. Resistant to mastitis depends upon classification by three significant factors: the animal's genetics, physiological condition, and environment where the animal is present [45]. A researcher in his study reported that we could divide resistance to mastitis into two groups: direct control and indirect control. He said that with the help of direct measures, we could control mastitis by identifying the infection and enhancing the immune system of animals to control this infection. In contrast, with indirect control or measure, we have to predict the pathogenic status of the udder by observing the parameter of inflammation that includes somatic cell count (SCC) and conductivity [45]. It is also reported that resistance to mastitis is a complex mechanism in which different factor play their role, like Bald (bovine leukocyte adhesion deficiency), lactoferrin and lysozyme [45]. Similarly, another researcher reported that lactoferrin is an iron-binding protein with bacteriostatic properties that protect the mammary gland [46]. At the same time, lysozyme cleaves the bacteria's cell wall and helps control bacterial infection [45].

A researcher in his research reported that the CD18 gene is linked with Bald in Holstein Friesian breed. He reported that the CD18 gene encodes the B-subunit of IFAM, an integrin family of ad-

hesion molecules important to produce resistance against mastitis. He reported that harmful alleles cause no expression of these molecules, and animals having homozygous bad alleles lead to abnormal diapedesis of leukocytes, making animals more sensitive to any infection [47,48]. A study of mastitis for genetics was done a long time ago. Many studies are still required on genetics and how mastitis is connected with genetics, and many other factors will come forward. Scientists are continuously working on two factors that are somatic cell count and subclinical mastitis, to improve resistance to mastitis. In future, QTL detection, epidemiological models and genetic analysis will be helpful in studying genetic relation to mastitis.

### Treatment of mastitis during lactation

Therapeutic response of the cows can be checked by victimization individual somatic cell count, California Mastitis Test (CMT), and bacteriological samples in herds with contagious mastitis. Treating subclinical udder inflammation with antimicrobials is mostly not economical throughout lactation as a result of price of treatment is high and had effectiveness poor [19].

### Controlling contagious mastitis

Staphylococcus aureus infections is the largest mastitis downside of farm animals. Most of the researcher in his research reported that this pathogen is highly contagious and transfer from one animal to other animal very rapidly [19]. With antibiotic therapy during lactation, cure rate is incredibly low and plenty infected animal become chronic case and had to be culled. A researcher in his researcher reported that antibiotic had good result against Strep. Agalactiae and we can control it with better management and treatment protocols that is dipping of teat and dry animal protocols. Strep dysgalactiae might live nearly anyplace. It will enter into the mammary gland and are moderately at susceptible of antibiotics [23].

### Controlling environmental mastitis

It is often achieved by decreasing the amount of microorganism to which the teat end is exposed. The animal's setting need to be clean and dry. There should be proper removal of manure, and scraping should be done after every milking to decrease the chances of mastitis and prevent the contact of mud and stagnant water with animal. Calving pen must be clean and hygienic and must be sprayed with germicidal drugs on day basis. Post milking dipping of teat with an antiseptic solution is good practice to control mastitis. To control mastitis during dry period, using germicidal, attempts have been unsuccessful. Proper antibiotic therapy is need for all animals at drying off. It will help us to control environment streptococci during the early dry period [23].

### Discussion and Conclusion

Mastitis is one of the crucial and widespread condition in both large ruminant as well as small ruminant. It had a major impact on

dairy industry is and is the reason of major profit loss. By proper management practices and dry cow therapy protect the cow from mastitis. Behavioral changes help us in recognizing illness in animals. Dairy cows expressing the signs of sickness behavior, such as a decrease in feeding, ruminating, and self-grooming during the initial days after mastitis induction can help us in the diagnosis of animal. So, we can use behavioral changes as an indicator of illness in early lactation cows. Monitoring of somatic cell counts and prompt identification and treatment of mastitis in dairy animals help in the reduction of mastitis and less treatment cost. It is reported that 70 percent of mastitis cause by environmental pathogen can be controlled by Dry animal therapy. Streptococcus agalactiae respond well to antibiotic therapy and can be eradicated from dairy herds with good mastitis control practices which include including teat dipping and dry animal treatment. Mastitis is directly related to milker man so we can control it by hygienic practice and better management.

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### Conflict of Interest

None.

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### Bibliography

1. Abera M., et al. "Isolation and identification of Staphylococcus aureus from bovine mastitic milk and their drug resistance patterns in Adama town, Ethiopia". *Journal of Veterinary Medicine and Animal Health* 2.3 (2010): 29-34.
2. Ali HM., et al. "Effects of natural environment on reproductive histo-morphometric dynamics of female dromedary camel". *Animal Reproduction Science* 181 (2017): 30-40.
3. AL-Samawy ERM., et al. "Histological and histochemical study on the large intestine of one-humped camel in Iraq". *Asian Journal of Agriculture and Biology* 7 (2019): 373-380.
4. Cady RA., et al. "Factors affecting performance of Nili-Ravi buffaloes in Pakistan". *Journal of Dairy Science* 66.3 (1983): 578-586.
5. Chaudhry HR., et al. "Bacteriology of Sub-Clinical Mastitis in the Dairy Buffaloes Maintained at Private Farms of Yazman, Distt. Bahawalpur". *Biologia (Pakistan)* 59.2 (2013): 259-262.
6. Chemweno VJ., et al. "PPR in camels: sero-prevalence and socio-economics". *International Journal of Veterinary Science* 8.2 (2019): 84-88.



7. EL-Hallawany HA., *et al.* "IMMUNO-HISTOMORPHOMETRIC STUDIES AND THE EFFECT OF SOME ANTIBIOTIC ALTERNATIVES ON SHE-CAMEL STAPHYLOCOCCUS MASTITIS". *Assiut Veterinary Medical Journal* 64.157 (2018): 99-119.
8. Government of Pakistan, 2007-2008. Pakistan Economic Survey. Economic Advisor's Wing, Ministry of Finance, Islamabad, Pakistan (2008).
9. He W., *et al.* "Prevalence, etiology, and economic impact of clinical mastitis on large dairy farms in China". *Veterinary Microbiology* 242 (2020): 108570.
10. Hota., *et al.* "Bovine Mastitis: Pathogenesis and Susceptibility". *Agro Economist* (2020): 107.
11. Hussain R., *et al.* "Changes in some biochemical parameters and somatic cell counts in the milk of buffalo and cattle suffering from mastitis". *Pakistan Veterinary Journal* 32.3 (2012): 418-421.
12. Hussain R., *et al.* "Risks factors associated with subclinical mastitis in water buffaloes in Pakistan". *Tropical Animal Health and Production* 45.8 (2013): 1723-1729.
13. Hussain R., *et al.* "Mastitis and associated histo-pathological consequences in the context of udder morphology". *International Journal of Agriculture and Biology* 14.6 (2012).
14. Hussain R., *et al.* "Clinico-hematological and oxidative stress status in Nili Ravi buffaloes infected with Trypanosoma evansi". *Microbial Pathogenesis* 123 (2018): 126-131.
15. Hussain R., *et al.* "Investigation of Different Serotypes of FMDV in Vaccinated Buffaloes (Bubalus bubalis) in Southern Areas of Punjab Province, Pakistan". *Pakistan Veterinary Journal* 40.1 (2020).
16. Hussain R., *et al.* "Clinical, pathologicoanatomic and mycological studies of aspergillosis in ostrich (Struthio camelus)". *Asian Journal of Agriculture and Biology* 8.4 (2020): 386-391.
17. Ibrahim AM., *et al.* "Epidemiology and microbiological studies on mastitis in she-camels". *International Journal of Microbiology* 2 (2011): 18-27.
18. Idriss SE., *et al.* "Mastitis pathogens and their resistance against antimicrobial agents in dairy cows in Nitra, Slovakia, Slovak". *Journal of Animal Science* 47.1 (2014): 33-38.
19. Johnson RW. "The concept of sickness behavior: a brief chronological account of four key discoveries". *Veterinary Immunology and Immunopathology* 87.3-4 (2002): 443-450.
20. Jones GM. "Understanding the basics of mastitis". *Virginia Cooperative Extension*. Publication No. 404-233. Virginia State University, USA (2006): 1-7.
21. Kemp MH., *et al.* "Animal-based measurements of the severity of mastitis in dairy cows". *Veterinary Record* 163.6 (2008): 175-179.
22. Khan A., *et al.* "Molecular analysis of virulent genes (coa and spa) of Staphylococcus aureus involved in natural cases of bovine mastitis". *Pakistan Journal of Agricultural Sciences* 50 (2013): 739-743.
23. Khan MZ and Khan A. "Basic facts of mastitis in dairy animals: a review". *Pakistan Veterinary Journal* 26.4 (2006): 204.
24. Mahmood F., *et al.* "Patho-bacteriological investigation of an outbreak of Mycoplasma bovis infection in calves-Emerging stealth assault". *Microbial Pathogenesis* 107 (2017): 404-408.
25. Mohammadian B. "The effect of subclinical mastitis on lactate dehydrogenase in dairy cows". *International Journal of Animal and Veterinary Advances* 3.3 (2011): 161-163.
26. Patnaik S., *et al.* "Biochemical characterization and antibiogram of Staphylococcal microorganisms associated with subclinical mastitis in lactating crossbred cows". *Animal Science Reporter* 8.4 (2014): 123-129.
27. Paulrud CO. "Basic concepts of the bovine teat canal". *Veterinary Research Communications* 29.3 (2005): 215-224.
28. Pyörälä S. "Treatment of mastitis during lactation". *Irish Veterinary Journal* 62.4 (2009): S40.
29. Pyorala S. "Indicators of inflammation in the diagnosis of mastitis". *Veterinary Research* 34 (2003): 565-567.
30. Qayyum A., *et al.* "Investigation of milk and blood serum biochemical profile as an indicator of sub-clinical mastitis in Cholistani cattle". *Pakistan Veterinary Journal* 36.3 (2016): 275-279.
31. Royster E and Wagner S. "Treatment of mastitis in cattle". *Veterinary Clinics: Food Animal Practice* 31.1 (2015): 17-46.
32. Schabauer A., *et al.* "The relationship between clinical signs and microbiological species, spa type, and antimicrobial resistance in bovine mastitis cases in Austria". *Veterinary Microbiology* 227 (2018): 52-60.
33. Sharma N. "Epidemiological investigation on sub-clinical mastitis in dairy animals: Role of vitamin-E and selenium supplementation on its control in cattle (Doctoral dissertation, CHHATTISGARH KAMDHENU VISHWAVIDYALAYA, DURG) (2003).
34. Siivonen J., *et al.* "Impact of acute clinical mastitis on cow behaviour". *Applied Animal Behaviour Science* 132.3-4 (2011): 101-106.

35. Svensson C., *et al.* "Effects of housing, management, and health of dairy heifers on first-lactation udder health in southwest Sweden". *Journal of Dairy Science* 89 (2006): 1990-1999.
36. Tiwari JG., *et al.* "Trends in therapeutic and prevention strategies for management of bovine mastitis: an overview". *Journal of Vaccines and Vaccination* 4.1 (2013): 1-11.
37. Yousaf M., *et al.* "Effect of infusions of non-antibiotic antibacterials alone and in combination with cephradine on milk yield of buffaloes affected with clinical mastitis". *Pakistan Veterinary Journal* 30 (2010): 39-43.
38. Zafar A., *et al.* "Seroprevalence of *Fasciola hepatica* in small ruminants of District Chakwal, Punjab, Pakistan". *Pakistan Veterinary Journal* 39.1 (2019).
39. Zenebe N., *et al.* "Study on bovine mastitis and associated risk factors in Adigrat, Northern Ethiopia". *African Journal of Microbiology Research* 8.4 (2008): 327-333.
40. Zhao X and Lacasse P. "Mammary tissue damage during bovine mastitis: causes and control". *Journal of Animal Science* 86 (2008): 57-65. Abera M., *et al.* "Isolation and identification of *Staphylococcus aureus* from bovine mastitic milk and their drug resistance patterns in Adama town, Ethiopia". *Journal of Veterinary Medicine and Animal Health* 2.3 (2010): 29-34.
41. Dey, D., Sharma, B. and Mondal, S., 2019. Nutritional approach to prevent mastitis of dairy cattle. *Environment and Ecology*, 37(1B), pp.344-348.
42. Politis, I., Bizelis, I., Tsiaras, A. and Baldi, A., 2004. Effect of vitamin E supplementation on neutrophil function, milk composition and plasmin activity in dairy cows in a commercial herd. *Journal of dairy research*, 71(3), pp.273-278.
43. Babir, M., Atif, F.A. and Rehman, A.U., 2017. Effect of pre-partum dietary cation-anion difference on the performance of transition Sahiwal cattle. *JAPS: Journal of Animal & Plant Sciences*, 27(6).
44. Sordillo, L.M., 2016. Nutritional strategies to optimize dairy cattle immunity. *Journal of dairy science*, 99(6), pp.4967-4982.
45. Rupp, R. and Boichard, D., 2003. Genetics of resistance to mastitis in dairy cattle. *Veterinary research*, 34(5), pp.671-688.
46. Seyfert, H.M., Henke, M., Interthal, H., Klussmann, U., Koczan, D., Natour, S., Pusch, W., Senft, B., Steinhoff, U.M., Tuckoricz, A. and Hobom, G., 1996. Defining candidate genes for mastitis resistance in cattle: the role of lactoferrin and lysozyme. *Journal of animal breeding and genetics*, 113(1-6), pp.269-276.
47. Shuster, D.E., Kehrli, M.E., Ackermann, M.R. and Gilbert, R.O., 1992. Identification and prevalence of a genetic defect that causes leukocyte adhesion deficiency in Holstein cattle. *Proceedings of the National Academy of Sciences*, 89(19), pp.9225-9229.
48. Kehrli Jr, M.E., Schmalstieg, F.C., Anderson, D.C., Van Der Maaten, M.J., Hughes, B.J., Ackermann, M.R., Wilhelmssen, C.L., Brown, G.B., Stevens, M.G. and Whetstone, C.A., 1990. Molecular definition of the bovine granulocytopeny syndrome: identification of deficiency of the Mac-1 (CD11b/CD18) glycoprotein. *American journal of veterinary research*, 51(11), pp.1826-1836.