STM JOURNALS

Emerging Trends in
Metabolites

ISSN: 3049-1916
Volume 2, Issue 1, 2025
January–June
DOI (Journal): 10.37591/ETM

https://journals.stmjournals.com/etm

Review ETM

Colostrum-Driven Epigenetic Programming in Dairy Cows: A Pathway to Optimal Reproductive Health

Md. Emran Hossain*

Abstract

Colostrum is a vital nutritional source for neonatal calves, providing immune support and essential growth factors. Recent research suggests that colostrum's impact extends beyond immediate immunological protection, influencing long-term reproductive health through epigenetic modifications. In dairy heifers, early-life exposure to high-quality colostrum may program the developing reproductive system, affecting ovarian function, uterine health, and overall fertility. The components of colostrum, including hormones, growth factors, and bioactive peptides, can induce epigenetic changes that can alter gene expression patterns involved in reproductive tissue development and hormonal regulation. These modifications can potentially enhance reproductive efficiency by optimizing ovarian reserve, improving follicular development, and promoting uterine health. This review explores the mechanisms through which colostrum-driven epigenetic programming influences the reproductive health of dairy heifers. It highlights the critical role of colostrum in regulating genes associated with puberty onset, ovarian function, and reproductive longevity. Moreover, it examines the interaction between colostrum nutrients and the gut-reproductive axis, shedding light on how early gut health impacts hormonal pathways governing reproduction. Understanding these processes could provide new strategies for improving fertility and productivity in dairy herds. By optimizing colostrum management practices, it may be possible to enhance reproductive outcomes, ensuring sustainable dairy farming practices and long-term herd performance.

Keywords: Colostrum, dairy heifers, endocrine regulation, epigenetic programming, fertility, immune modulation, ovarian function, puberty onset

INTRODUCTION

Colostrum is the first milk produced by dairy cows after parturition, rich in immunoglobulins, growth factors, hormones, and bioactive molecules. It plays a pivotal role in supporting neonatal health, particularly by providing passive immunity to protect against infections during the early days of life [1]. While its primary function is widely recognized in terms of immune protection and early development, emerging evidence suggests that colostrum's impact extends beyond immediate health benefits. Increasingly, research indicates that the bioactive components of colostrum may influence long-term physiological processes, including reproductive development and function in heifers [2].

***Author for Correspondence**
Md. Emran Hossain
E mail: emran@cvasu.ac.bd

Professor, Department of Animal Science and Nutrition, Chattogram Veterinary and Animal Sciences University, Khulshi, Chattogram, Bangladesh.

Received Date: February 28, 2025
Accepted Date: March 06, 2025
Published Date: March 19, 2025

Citation: Md. Emran Hossain. Colostrum-Driven Epigenetic Programming in Dairy Cows: A Pathway to Optimal Reproductive Health. Emerging Trends in Metabolites. 2025; 2(1): 35–51p.

The reproductive system of dairy heifers undergoes significant maturation during the early stages of life, setting the stage for future fertility. Colostrum, with its rich composition of hormones and growth factors, may serve as a key modulator of reproductive health by influencing the development of the ovaries, uterus, and other reproductive tissues. This study explores the potential for colostrum-driven epigenetic

programming, where early exposure to colostrum could modify gene expression patterns in reproductive tissues. These epigenetic changes may impact ovarian function, uterine development, and overall fertility by optimizing tissue growth, hormonal regulation, and metabolic pathways that govern reproduction.

The novelty of this study lies in its focus on the epigenetic mechanisms through which colostrum affects reproductive health in dairy heifers. While the role of colostrum in immune function is well-established, its influence on epigenetic programming of the reproductive system remains underexplored. This research proposes a new perspective by linking colostrum's nutritional and bioactive components to long-term reproductive outcomes through epigenetic modifications. Understanding these underlying mechanisms offers the potential to develop novel strategies for improving fertility and productivity in dairy herds, thereby ensuring sustainable dairy farming practices. By focusing on the developmental period immediately after birth, this study paves the way for enhancing reproductive efficiency through improved colostrum management.

IMMUNOLOGICAL SUPPORT

Maternal Immunoglobulin Transfer

Transfer of maternal immunoglobulins via colostrum reduces reproductive tract infections in calves. The antibodies provided through colostrum strengthen the immune system, helping to fight off pathogens that may cause reproductive issues [3]. This early immunological support ensures that the reproductive tract remains free from infections, which is essential for maintaining reproductive health and fertility in dairy heifers.

Colostral Antibodies and Ovarian Health

Colostral antibodies enhance ovarian resilience by protecting the ovaries from infections and inflammatory responses. These antibodies play a vital role in maintaining ovarian function and health. By reducing the risk of infection, colostrum ensures that the ovaries can perform their essential reproductive functions, thus improving the fertility and overall reproductive success of heifers as they mature.

Passive Immunity Against Uterine Inflammation

Passive immunity provided by colostrum helps prevent uterine inflammation in calves [4]. The antibodies transferred to the calf assist in minimizing the chances of uterine infections and inflammatory conditions. This protection ensures that the uterus remains healthy, promoting proper embryonic implantation and reducing the risk of complications in future pregnancies, ultimately supporting optimal reproductive health.

Immunoglobulins and Tissue Integrity

Immunoglobulins in colostrum help support reproductive tissue integrity by shielding reproductive organs from infections and oxidative damage. These immune components contribute to the protection and repair of tissues within the reproductive system, ensuring that the structures remain intact and functional. This is crucial for maintaining long-term reproductive health and fertility in dairy heifers.

Cytokine Response and Ovarian Health

Enhanced cytokine responses due to colostrum intake improve ovarian health by regulating immune activity. Cytokines help control inflammation, ensuring that the ovaries remain protected from tissue damage [5]. Proper cytokine balance contributes to ovarian health, ensuring the ovaries function optimally for reproductive success, including regular estrous cycles and successful fertilization.

Protection Against Systemic Diseases

Colostrum provides essential antibodies that protect calves from systemic diseases that could negatively affect reproduction. By offering passive immunity, colostrum ensure that the calf's immune system is strong enough to resist infections that may compromise reproductive function [4]. This protection is vital for the long-term reproductive health and fertility of the dairy cow.

Antibodies Minimize Inflammation

Colostrum's antibodies help minimize inflammation in reproductive organs by neutralizing pathogens and modulating immune responses [6]. This reduction in inflammation is essential for maintaining the integrity and function of the reproductive system. Less inflammation leads to healthier reproductive tissues, enhancing the chances of successful breeding, pregnancy, and overall reproductive health.

Colostrum and Reproductive Failure Prevention

Colostrum prevents reproductive failure by providing immunological support to protect against infections and inflammation. The antibodies transferred through colostrum ensure that the reproductive organs remain protected and functional. This early immune boost reduces the likelihood of complications, such as uterine infections and ovarian dysfunction, which could lead to reproductive failures in the future.

Tissue Repair and Immune Support

Immunoglobulins from colostrum promote tissue repair in the reproductive system by stimulating the regeneration of damaged tissues. This repair mechanism ensures that reproductive organs, including the ovaries and uterus, remain healthy and functional. A well-repaired reproductive system is critical for maintaining fertility, supporting regular estrous cycles, and ensuring the success of future pregnancies.

STRENGTH AND REPRODUCTIVE PROTECTION

Immune

Increased immune strength provided by colostrum protects the reproductive tract from damage. A stronger immune system helps prevent infections and inflammation, ensuring the reproductive organs remain healthy and intact [7]. This immune support ensures that the heifer has a better chance of successful conception and long-term reproductive health, contributing to higher fertility and productivity.

Endocrine Influences

Regulation of Hypothalamic-Pituitary-Gonadal Axis

Colostral hormones play a crucial role in regulating the hypothalamic-pituitary-gonadal (HPG) axis in calves. These hormones help in the development and function of the reproductive system by controlling the release of key gonadotropins. This regulation ensures proper reproductive tract development, hormonal balance, and supports future fertility in heifers, optimizing their reproductive efficiency.

Estrogen and Ovarian Development

Estrogen in colostrum influences ovarian development by stimulating follicular growth and maturation [8]. It promotes the formation of the primary reproductive structures, ensuring that the ovaries are prepared for future reproductive cycles. This hormonal influence plays an essential role in the calf's ability to reach puberty and develop reproductive competence as they mature into heifers.

Progesterone and Uterine Lining

Progesterone, present in colostrum, supports the formation and maintenance of the uterine lining in calves [9]. This hormone prepares the uterus for embryo implantation and subsequent pregnancy. By supporting uterine tissue development, progesterone ensures the reproductive tract is ready for reproductive events, such as conception, thereby improving the chances of successful pregnancies later in life.

Growth Hormones and Follicular Development

Growth hormones found in colostrum enhance the development of ovarian follicles [10]. These hormones stimulate the growth and maturation of oocytes, contributing to the creation of a healthy ovarian reserve. By promoting follicular development, growth hormones ensure that the ovaries are

prepared to produce high-quality oocytes, enhancing fertility in dairy heifers as they reach reproductive maturity.

Insulin-Like Growth Factors and Ovarian Maturation

Insulin-like growth factors (IGFs) present in colostrum play an important role in ovarian maturation. IGFs support the growth of ovarian follicles and promote the development of oocytes [11]. These factors help in achieving optimal ovarian function, ensuring that the reproductive system is primed for successful conception and healthy offspring production, thus enhancing fertility in heifers.

Cortisol and Stress-Induced Reproduction

Cortisol, present in colostrum, plays a role in regulating stress-induced reproductive issues in calves [12]. This hormone helps manage the effects of environmental and physiological stress on reproductive health. By moderating stress responses, cortisol ensures that reproductive function remains intact, preventing stress-induced infertility and promoting long-term reproductive success in heifers.

RELAXIN AND UTERINE GROWTH

Relaxin, a hormone present in colostrum, supports uterine tissue growth and relaxation. It promotes the growth of uterine tissues, enhancing uterine capacity for future pregnancies. By stimulating smooth muscle development, relaxin ensures the uterus can properly accommodate an embryo and maintain a healthy pregnancy, contributing to improved reproductive outcomes in dairy heifers.

Hormonal Stimulation of Gonadotropins

Colostral hormones stimulate the release of gonadotropic hormones, which are essential for the regulation of ovarian and reproductive functions. Gonadotropins control the ovarian cycles and follicular development, ensuring that the reproductive system operates optimally [13]. By influencing the release of these hormones, colostrum helps establish a functional reproductive system, enhancing fertility and successful breeding in dairy heifers.

Prostaglandins and Ovarian Function

Prostaglandins present in colostrum enhance ovarian function by supporting follicular development and luteal regression. They play a key role in regulating the estrous cycle and maintaining the balance of reproductive hormones. By supporting these processes, prostaglandins ensure proper ovarian function, which is critical for successful reproduction and fertility in dairy heifers.

Bioactive Peptides and Hormone Signaling

Bioactive peptides in colostrum improve reproductive hormone signaling by modulating the activity of receptors involved in the hormonal cascade [2]. These peptides help enhance the responsiveness of reproductive tissues to hormonal signals, improving reproductive efficiency. By optimizing hormonal signaling, bioactive peptides ensure the proper development of reproductive organs and enhance fertility outcomes in dairy heifers.

NUTRITIONAL EFFECTS

High Protein and Follicular Development

High protein content in colostrum plays a vital role in the development of ovarian follicles in calves. Protein provides essential building blocks for cellular growth and function, particularly in the ovaries [14]. This supports the maturation of healthy follicles, which are critical for optimal reproductive performance and fertility. Adequate protein intake helps ensure that heifers have a strong ovarian reserve for future reproduction.

Essential Amino Acids and Uterine Growth

Essential amino acids present in colostrum support the growth and development of uterine tissues in calves. These amino acids are necessary for protein synthesis, which is crucial for uterine cell proliferation and tissue formation. By promoting uterine growth, essential amino acids ensure that the

reproductive tract is properly developed, enhancing the chances of successful pregnancies in dairy heifers.

Colostral lipids and Hormone Synthesis

Colostral lipids improve reproductive hormone synthesis in calves [15]. Lipids provide the necessary fatty acids and cholesterol required for the production of steroid hormones like estrogen and progesterone [16]. These hormones are vital for the regulation of the estrous cycle, follicular development, and overall reproductive health. By supporting hormone synthesis, colostrum plays a key role in optimizing reproductive outcomes.

Vitamins and Reproductive Tissue Functionality

Vitamins A, D, and E present in colostrum enhance the functionality of reproductive tissues. Vitamin A supports cell differentiation and tissue integrity, while Vitamin D plays a crucial role in calcium metabolism, essential for uterine health [17, 18]. Vitamin E, an antioxidant, protects reproductive tissues from oxidative damage. Together, these vitamins support the overall health and functionality of the reproductive system.

MINERALS AND OVARIAN ACTIVITY

Minerals absorbed from colostrum support ovarian activity and overall reproductive health. Minerals like magnesium, copper, and manganese are involved in enzyme activation and the maintenance of reproductive tissue integrity [19, 20]. These minerals contribute to ovarian function, supporting healthy follicle development and ensuring optimal reproductive performance in heifers by maintaining proper hormonal balance.

Calcium and Uterine Contractions

Calcium in colostrum promotes uterine contractions, which are essential for the effective expulsion of the placenta after parturition. Calcium is also critical for the smooth muscle function in the uterus, supporting uterine health [21, 22]. By ensuring proper calcium levels, colostrum contributes to the development of a well-functioning reproductive tract, enhancing fertility and the chances of successful pregnancies.

Zinc and Hormone Regulation

Zinc found in colostrum aids in the regulation of reproductive hormones by influencing their synthesis and action. It plays a vital role in maintaining hormonal balance, which is crucial for the proper functioning of the reproductive system. Adequate zinc levels ensure that heifers experience optimal hormonal regulation, improving ovarian function and reproductive success.

Selenium and Oxidative Stress Protection

Selenium in colostrum protects reproductive cells from oxidative stress. It acts as an antioxidant, neutralizing harmful free radicals that can damage reproductive cells and tissues [23]. By reducing oxidative stress, selenium helps preserve the integrity of ovarian and uterine cells, ensuring the long-term health and functionality of the reproductive system in heifers.

Energy-Rich Colostrum and Follicular Growth

Energy-rich colostrum promotes the growth and maturation of ovarian follicles in calves. The high-energy content provides the necessary fuel for metabolic processes that support follicular development. Adequate energy intake ensures that heifers can develop healthy follicles, improving their chances of successful ovulation and conception, which is essential for optimal reproductive health.

Carbohydrates and Metabolic Pathways

Carbohydrates in colostrum enhance the metabolic pathways involved in reproduction. They provide a primary source of energy that supports cellular processes critical for reproductive health [21]. By enhancing metabolic activity, carbohydrates help regulate hormonal balance, support follicular growth,

and promote the overall efficiency of reproductive processes, contributing to better fertility and reproductive outcomes in heifers.

GUT-REPRODUCTIVE AXIS INTERACTIONS

Gut Barrier and Inflammation

Colostrum strengthens the gut barrier, reducing systemic inflammation [24]. A strong gut barrier prevents harmful pathogens from entering the bloodstream, which can trigger an inflammatory response that negatively impacts the reproductive system. By minimizing systemic inflammation, colostrum ensures a healthier environment for reproductive tissues, promoting optimal ovarian and uterine function and enhancing overall fertility in heifers.

Gut Health and Hormone Synthesis

Improved gut health, supported by colostrum, plays a key role in hormonal synthesis. A healthy gut facilitates the production of essential hormones, including those involved in reproduction. Hormonal balance is crucial for the regulation of the estrous cycle and follicular development, ensuring that dairy heifers experience optimal reproductive function and are more likely to conceive successfully.

Gut Microbiota and Nutrient Absorption

The gut microbiota in colostrum-fed calves improves nutrient absorption for reproductive development. Beneficial bacteria in the gut break down nutrients, making them more bioavailable, which supports the growth and maturation of reproductive organs [25]. Enhanced nutrient absorption ensures that calves receive the essential vitamins, minerals, and amino acids needed for healthy ovarian and uterine development, ultimately improving reproductive health.

Endotoxins and Ovarian Function

Reduced endotoxins in colostrum benefit ovarian function by preventing systemic infections and inflammation. Endotoxins from harmful bacteria can negatively affect ovarian tissue, impairing follicular development and hormone regulation. By reducing endotoxin levels, colostrum promotes a healthier reproductive system, ensuring better ovarian health and function, which is crucial for fertility and long-term reproductive success.

BIOACTIVE PEPTIDES AND HORMONE RELEASE

Bioactive peptides in colostrum support hypothalamic hormone release, which is essential for the regulation of reproductive hormones. These peptides influence the hypothalamus-pituitary-gonadal axis, stimulating the release of gonadotropins and other hormones involved in follicular growth and ovulation. By enhancing hormone release, colostrum ensures that heifers have a well-regulated reproductive system, improving fertility outcomes.

Gut Integrity and Reproductive Inflammation

Improved gut integrity, promoted by colostrum, reduces reproductive inflammation. A healthier gut prevents the entry of harmful bacteria and endotoxins, which can trigger inflammatory responses that affect reproductive tissues [26]. Reducing gut-induced inflammation protects ovarian and uterine health, supporting better fertility, hormone function, and overall reproductive success in dairy heifers.

NUTRIENT UPTAKE AND OVARIAN RESERVES

Enhanced nutrient uptake, facilitated by a healthy gut, supports ovarian reserves. The efficient absorption of key nutrients like vitamins, minerals, and amino acids ensures that the ovaries develop optimally and maintain a healthy follicular reserve. This supports future reproductive cycles, improving the chances of successful ovulation and conception, and enhancing the overall fertility potential of dairy heifers.

Probiotics and Reproductive Immunity

Probiotics from colostrum modulate reproductive immunity by promoting the growth of beneficial gut bacteria. These beneficial microbes strengthen the immune system, enhancing the body's ability to

fight off infections that could impair reproductive health. A balanced immune system reduces the risk of reproductive tract infections, ensuring a healthier reproductive environment for heifers.

Gut Bacteria and Estrogen Metabolism

Healthy gut bacteria, supported by colostrum, promote estrogen metabolism, which is essential for reproductive health. The gut microbiota aids in the conversion of estrogen into its active forms, regulating the estrous cycle and ovarian function. Proper estrogen metabolism ensures that heifers maintain hormonal balance, promoting optimal follicular development and improving fertility outcomes.

Prebiotics and Gut-Hormone Interactions

Prebiotics in colostrum influence gut-hormone interactions, promoting better reproductive health. Prebiotics serve as food for beneficial gut bacteria, supporting a healthy gut microbiota [27]. This, in turn, positively affects the synthesis and release of reproductive hormones, including those that regulate the estrous cycle. By improving gut-hormone interactions, prebiotics enhance the overall fertility and reproductive success of heifers.

METABOLIC PROGRAMMING

Hypothalamic Function

Early nutrient intake, particularly through colostrum, shapes hypothalamic function, which is crucial for the regulation of reproductive hormones. Nutrients in colostrum affect the hypothalamus' ability to produce hormones that control the pituitary gland, thus influencing ovulation and estrous cycle regulation [28]. Proper hypothalamic function ensures effective hormone signaling for reproductive health and improved fertility in dairy heifers.

Metabolic Efficiency and Fertility

Colostrum promotes metabolic efficiency by providing key nutrients that help optimize energy balance and nutrient utilization. By supporting efficient metabolism, colostrum ensures that the body has the necessary energy for reproductive processes. This efficiency influences fertility by ensuring that the energy required for ovarian function and egg maturation is readily available, improving reproductive outcomes in dairy heifers.

Insulin Sensitivity and Hormones

Nutrients in colostrum regulate insulin sensitivity, which is closely linked to reproductive hormone regulation. Insulin plays a role in ovarian function by influencing the availability of glucose and other metabolic substrates necessary for hormone production. Proper insulin sensitivity ensures the optimal functioning of reproductive hormones, contributing to better follicular development and hormonal balance in dairy heifers.

Energy Metabolism and Puberty

Programming energy metabolism through early nutrient intake, such as colostrum, supports the timely onset of puberty. Early-life nutrition influences the efficiency of energy utilization in the body, which in turn impacts hormonal signaling pathways that regulate puberty [29]. This early programming ensures that dairy heifers reach puberty at the appropriate time, optimizing fertility and reproductive health.

Amino Acids and Ovarian Activity

Amino acids in colostrum play a critical role in modulating future ovarian activity by supporting the synthesis of proteins essential for ovarian development [2]. These amino acids contribute to follicular development and the production of key reproductive hormones. Proper amino acid availability ensures that heifers have healthy ovaries, which supports optimal fertility and reproductive success.

Nutritional Programming and Longevity

Nutritional programming via colostrum impacts reproductive longevity by influencing the development of reproductive tissues and hormone regulation. Early nutrient intake helps set the foundation for long-term reproductive health by ensuring the proper function of ovaries and the hormonal system. This early programming reduces the risk of reproductive dysfunction later in life, improving the heifer's fertility over time.

METABOLIC STRESS REDUCTION

Colostrum reduces metabolic stress that could otherwise impair reproductive function [30]. Stress can lead to hormonal imbalances and poor ovarian health, but the nutrients in colostrum help mitigate these effects by improving metabolic regulation. Reduced metabolic stress supports the optimal function of the reproductive system, leading to improved fertility and reduced chances of reproductive failure.

Metabolic Shifts and Reproductive Success

Early metabolic shifts influenced by colostrum intake play a significant role in shaping reproductive success. Proper nutrient programming during the neonatal stage affects the body's ability to metabolize energy and hormones [31]. These early shifts ensure that metabolic pathways are optimized for reproductive health, leading to better follicular development, ovulation, and overall reproductive outcomes.

Energy Balance and Follicle Growth

Improved energy balance supported by colostrum ensures that dairy heifers have adequate resources for ovarian follicle growth. A balanced energy state is essential for follicular development and maturation, as it provides the necessary nutrients for cellular processes. By ensuring proper energy balance, colostrum promotes the growth of healthy follicles and enhances reproductive success in dairy heifers.

Epigenetic Reprogramming

Epigenetic reprogramming driven by nutrients in colostrum enhances the expression of genes responsible for reproductive health. Early-life nutrition affects DNA methylation and histone modifications, which influence the expression of reproductive genes [32]. This reprogramming supports optimal ovarian function, hormonal regulation, and uterine health, contributing to better fertility and long-term reproductive health in dairy heifers.

IMMUNE-MODULATION

Cytokines and Ovarian Health

Anti-inflammatory cytokines present in colostrum help regulate ovarian health by reducing inflammation [33]. These cytokines protect ovarian tissues from immune system attacks and inflammatory damage, supporting follicular development and function. By maintaining a balanced immune response, cytokines contribute to healthy ovarian function, ensuring effective hormone production and enhanced fertility in dairy heifers.

T-cell Activation and Uterine Immunity

Colostrum plays a role in activating T-cells, which enhances uterine immunity. This T-cell activation strengthens the uterine immune system, preventing infections and promoting tissue health. A robust uterine immune response is crucial for maintaining reproductive health, as it supports the uterus in handling challenges, such as microbial infections and inflammatory conditions that could affect fertility.

Systemic Inflammation and Follicular Development

Reduced systemic inflammation, promoted by colostral nutrients, aids in the optimal development of ovarian follicles. Chronic inflammation can impair ovarian function, leading to poor follicle growth and decreased fertility [34]. By reducing systemic inflammation, colostrum helps ensure that the ovaries can function efficiently, supporting the development and maturation of healthy follicles that are essential for successful reproduction.

Immune Responses and Reproductive Health

Enhanced immune responses through colostrum intake improve the overall health of the reproductive tract [3]. A well-functioning immune system helps prevent infections, reduces inflammation, and supports tissue repair, which is essential for maintaining reproductive health. By improving immune function, colostrum creates a favorable environment for optimal fertility and reproductive success in dairy heifers.

Oxidative Damage Reduction

Colostrum reduces oxidative damage to reproductive tissues by providing antioxidants that neutralize harmful free radicals [23]. Oxidative stress can impair reproductive tissue integrity and function, leading to suboptimal fertility. The antioxidants in colostrum protect ovarian and uterine tissues, supporting healthy reproductive tissues and ensuring optimal conditions for fertilization and pregnancy.

Immune Peptides and Hormone Regulation

Immune-modulating peptides in colostrum regulate hormone production, contributing to the proper hormonal balance necessary for reproductive health. These peptides influence the secretion of hormones that control ovulation, estrous cycles, and uterine development. By supporting balanced hormone levels, immune-modulating peptides enhance fertility, promote healthy ovarian activity, and facilitate successful pregnancy.

Immunity and Uterine Microbial Balance

Strengthened immunity, supported by colostrum, helps maintain a balanced uterine microbiome. A healthy uterine microbiome is essential for preventing infections and inflammation that can negatively impact fertility. Colostrum-derived immune factors support the establishment and maintenance of beneficial microbes in the uterus, ensuring a healthy environment for embryo development and successful reproduction [1].

Antioxidants and Ovarian Integrity

The antioxidant properties of colostrum improve ovarian tissue integrity by protecting cells from oxidative damage. This is vital for preserving the health of ovarian follicles and maintaining hormonal balance. By preventing oxidative stress, antioxidants in colostrum support the functionality of the ovaries, ensuring that they remain capable of producing quality eggs and supporting successful reproduction.

Cytokines and Uterine Repair

Cytokines in colostrum promote uterine repair and resilience, aiding in the recovery of uterine tissues after injury or inflammation [35]. This repair process is essential for maintaining a healthy uterine environment that can support implantation and pregnancy. By promoting uterine tissue regeneration, cytokines help ensure the uterus remains functional and fertile for future reproductive cycles.

Immunity and Reproductive Tract Scarring

Immunity, enhanced by colostrum, aids in minimizing reproductive tract scarring that could interfere with fertility. Scarring from infections or injuries can impair the function of the uterus and ovaries, leading to reduced fertility. By strengthening the immune system, colostrum helps prevent scarring and supports the maintenance of healthy reproductive tissues, ensuring better reproductive outcomes in dairy heifers.

REPRODUCTIVE TRACT DEVELOPMENT

Growth Factors and Uterine Cells

Colostral growth factors stimulate the proliferation of uterine cells, which is crucial for the development of a healthy reproductive tract. This stimulation supports the growth and maintenance of uterine tissues, enhancing their ability to support pregnancy [33]. By promoting cell proliferation,

colostrum helps ensure the uterine lining is fully developed and functional, optimizing reproductive health.

Epithelial Growth and Uterine Lining

Enhanced epithelial growth, supported by colostral nutrients, improves the development of the uterine lining. A well-developed uterine lining is essential for embryo implantation and successful pregnancy [36]. By encouraging epithelial cell growth, colostrum contributes to the structural integrity of the uterus, ensuring a suitable environment for embryo development and increasing the chances of successful reproduction in dairy heifers.

Nutritional Support for Ovarian Growth

Nutritional support from colostrum aids the growth of ovarian tissue, which is essential for optimal reproductive function. Proper ovarian development is critical for producing high-quality eggs and maintaining hormonal balance. The nutrients in colostrum support the growth of healthy ovarian follicles, improving fertility and the likelihood of successful ovulation, fertilization, and pregnancy.

Bioactive Peptides and Follicular Differentiation

Bioactive peptides in colostrum promote follicular differentiation, which is necessary for the proper maturation of ovarian follicles. This process enhances the quality of eggs and improves the chances of successful fertilization. By supporting follicular development, colostrum helps optimize the reproductive capacity of dairy heifers, ensuring healthy ovarian activity and improved fertility outcomes.

Vascularization and Uterine Health

Improved vascularization, supported by colostrum, enhances uterine health by ensuring an adequate blood supply to the reproductive tissues. This increased blood flow delivers essential nutrients and oxygen, supporting uterine function and fertility. Healthy vascularization also promotes the repair and regeneration of uterine tissues, ensuring the uterus is prepared for successful pregnancy and optimal reproductive health.

Hormonal Support and Reproductive Tract

Colostrum provides hormonal support that strengthens reproductive tract structures, including the uterus and ovaries. These hormones play a crucial role in regulating the estrous cycle, ovulation, and uterine health. By maintaining proper hormonal levels, colostrum ensures that the reproductive tract remains in optimal condition, supporting fertility and ensuring successful reproductive cycles in dairy heifers.

Developmental Anomalies Prevention

Colostrum helps prevent developmental anomalies in reproductive tissues, ensuring the proper formation of the uterus and ovaries. Developmental defects in reproductive organs can lead to infertility or other reproductive complications [37]. By providing essential nutrients and growth factors, colostrum ensures that reproductive tissues develop correctly, enhancing the chances of successful reproduction and healthy offspring.

Proteins and Smooth Muscle Formation

Proteins in colostrum aid in the formation of smooth muscle in the uterus, which is necessary for uterine contraction during labor and proper uterine function throughout pregnancy. Smooth muscle formation supports the uterine walls, enabling efficient contractions during birth. By promoting uterine muscle development, colostrum helps ensure that the uterus functions properly, supporting both pregnancy and childbirth.

Uterine Gland Development

Enhanced uterine gland development, supported by colostrum, plays a key role in fertility [36]. Uterine glands produce secretions that nourish the embryo during early pregnancy, supporting its

growth and development. By promoting the growth and function of these glands, colostrum helps create an optimal environment for embryo implantation and early development, improving fertility and reproductive success in dairy heifers.

Ovarian Development and Fertility

Colostrum promotes robust ovarian development by supplying the necessary nutrients and growth factors that support follicular growth and maturation. Healthy ovarian development is essential for producing quality eggs and maintaining hormonal balance. By enhancing ovarian development, colostrum helps ensure optimal fertility, improving the chances of successful ovulation, fertilization, and pregnancy in dairy heifers.

DISEASE PREVENTION

Reproductive Tract Infection Prevention

Prevention of reproductive tract infections through colostral antibodies is vital for maintaining fertility. By reducing the risk of infections in the reproductive tract, colostrum helps maintain a healthy environment for ovulation, embryo implantation, and pregnancy. This protective effect ensures that fertility is preserved, promoting optimal reproductive outcomes in dairy heifers and reducing the need for veterinary intervention.

Reduced Neonatal Morbidity

Reduced neonatal morbidity, aided by colostrum, is essential for protecting the reproductive potential of dairy heifers [3]. Healthy calves are more likely to reach sexual maturity and develop strong reproductive systems. By strengthening immunity and preventing diseases in early life, colostrum helps ensure that neonatal calves can grow into productive, fertile animals, safeguarding their reproductive future.

Prevention of Systemic Infections

Colostrum plays a crucial role in preventing systemic infections that could adversely affect reproduction [1]. By providing passive immunity, colostrum helps protect the calf from pathogens that could impair reproductive health, such as infections that affect the ovaries or uterus. This protection helps ensure that the reproductive system remains functional, supporting long-term fertility and overall health.

Reduced Pelvic Inflammatory Conditions

Improved immunity through colostrum reduces the risk of pelvic inflammatory conditions, which can compromise reproductive health. By preventing these conditions, colostrum contributes to the maintenance of a healthy uterine environment, reducing the risk of infertility or complications during pregnancy. This immune support is crucial for ensuring that dairy heifers maintain optimal reproductive function throughout their lifespan.

Enhanced Disease Resistance

Colostrum enhances disease resistance, supporting long-term reproductive health by minimizing the risk of infections that could impair fertility [38]. Stronger immunity ensures that the reproductive system can effectively combat pathogens, maintaining uterine and ovarian health. This resistance is especially important for preventing diseases that can cause long-term reproductive issues, ensuring that dairy heifers maintain a productive and healthy reproductive life.

Antimicrobial Peptides for Ovarian Health

Antimicrobial peptides found in colostrum help prevent ovarian infections by inhibiting bacterial growth. This protection ensures the ovaries remain healthy, allowing for optimal follicular development and ovulation. By preventing infections that could damage ovarian tissue, colostrum supports long-term reproductive health and fertility, reducing the likelihood of ovarian-related infertility in dairy heifers.

Reduced Bacterial Invasion

Reduced bacterial invasion, facilitated by colostrum, benefits uterine health by minimizing the risk of infections that could lead to reproductive tract damage. Colostral antibodies neutralize harmful pathogens, preventing bacterial colonization in the uterus. This protection maintains a healthy uterine environment, supporting fertility and successful pregnancies, and minimizing the risk of conditions, such as uterine infections or endometritis.

Early Disease Prevention

Early disease prevention through colostrum ensures the health and longevity of the reproductive system [39]. By strengthening immunity during the neonatal period, colostrum reduces the risk of infections that can damage reproductive organs. This early intervention supports the long-term reproductive lifespan of dairy heifers, ensuring they remain fertile and capable of producing offspring throughout their productive life.

Minimizing Reproductive Organ Failure

Colostrum minimizes the risk of reproductive organ failure by providing essential nutrients and immune support. This protection helps maintain the structural integrity and function of the reproductive organs, ensuring they remain capable of supporting pregnancy. By reducing the risk of organ failure, colostrum supports long-term reproductive success, allowing dairy heifers to maintain fertility and contribute to herd productivity.

Ovarian Follicular Stability

Strong immunity, enhanced by colostrum, ensures ovarian follicular stability, which is essential for consistent ovulation and fertility. By preventing infections and inflammation in the ovaries, colostrum helps maintain the quality and number of ovarian follicles. This stability supports reproductive health, improves the chances of successful fertilization, and reduces the likelihood of reproductive failures in dairy heifers.

EPIGENETIC PROGRAMMING

Methylation Patterns and Reproduction

Methylation patterns influenced by colostrum shape reproductive outcomes by regulating genes involved in ovarian development. These patterns can impact the timing of puberty and overall fertility. Colostrum's role in modifying gene expression through epigenetic mechanisms ensures that the reproductive system develops optimally, promoting reproductive health and increasing the likelihood of successful reproduction in dairy heifers.

Regulation of Ovarian Development

Colostrum regulates genes that directly affect ovarian development, influencing the maturation and function of the ovaries. This regulation ensures that the ovaries are equipped to produce healthy eggs, promoting fertility and successful pregnancies. By modulating ovarian gene expression, colostrum supports long-term reproductive health, optimizing the potential for reproduction in dairy heifers as they mature.

Nutritional Programming of Puberty

Nutritional programming through colostrum influences the timing of puberty in dairy heifers by modulating the hormonal and metabolic systems. Proper nutrition early in life ensures the timely onset of puberty, which is crucial for reproductive success. Colostrum's influence on nutritional status helps regulate growth and reproductive hormone signaling, supporting optimal fertility in heifers [40].

Growth Factors and Fertility

Growth factors in colostrum drive gene expression that supports fertility by influencing the development of reproductive tissues [33]. These factors promote the growth of ovarian follicles, uterine lining, and other reproductive organs, which are essential for successful fertilization and pregnancy. By

stimulating these processes, colostrum helps ensure that dairy heifers reach reproductive maturity and maintain fertility.

Nutrient Impact on Reproductive Tissue

Early life nutrient intake, including colostrum, plays a vital role in improving the health of reproductive tissues. Nutrients in colostrum stimulate the growth and development of reproductive organs, strengthening their function [1]. This early nutritional impact on reproductive tissue health sets the foundation for optimal fertility and reproductive performance throughout the heifer's life.

Modulation of Receptor Expression

Colostrum modulates reproductive receptor expression, influencing how reproductive tissues respond to hormones [41]. By enhancing or altering the expression of key receptors in the ovaries and uterus, colostrum optimizes the sensitivity and effectiveness of reproductive hormones. This ensures that hormonal signals are properly received, supporting the fertility and reproductive health of dairy heifers.

Epigenetic Stability and Hormonal Balance

Epigenetic stability provided by colostrum ensures proper hormonal balance throughout the reproductive system. Stable gene expression allows for consistent hormone production and regulation, which is essential for fertility. By maintaining this balance, colostrum promotes regular ovulation cycles and proper uterine function, optimizing reproductive outcomes in dairy heifers.

Gene Regulation and Ovarian Reserve

Improved gene regulation, facilitated by colostrum, supports the maintenance and development of ovarian reserves. Proper regulation of genes involved in ovarian function helps maintain a healthy pool of eggs, supporting long-term fertility. By ensuring that the ovarian reserve is preserved, colostrum contributes to the reproductive success of dairy heifers throughout their lifespan.

Prevention of Epigenetic Defects

Colostral nutrients help prevent epigenetic defects in reproduction by promoting proper gene expression. These nutrients support the regulation of genes that govern ovarian development, hormonal regulation, and reproductive health. By preventing these defects, colostrum ensures the long-term fertility and reproductive success of dairy heifers, minimizing the risk of infertility and other reproductive disorders.

Hormone-Sensitive Gene Expression

Colostrum influences hormone-sensitive gene expression in the uterus, supporting tissue growth and development [42]. By regulating the expression of genes involved in uterine growth, colostrum helps ensure that the uterus is prepared for pregnancy. Proper gene expression in response to hormonal signals promotes uterine health and fertility, optimizing reproductive outcomes in dairy heifers.

BEHAVIOURAL IMPACTS

Stress Reduction and Hypothalamic-Pituitary Function

Stress reduction through colostrum intake enhances hypothalamic-pituitary function, supporting balanced hormone production and reproductive health. By minimizing stress, colostrum helps regulate the hormonal signals crucial for reproduction, improving overall fertility. This early-life influence on stress management ensures better reproductive performance as calves mature, contributing to optimal reproductive outcomes later in life.

Social Behaviour and Fertility

Colostrum-fed calves exhibit enhanced social behaviors that positively impact fertility [43]. Improved social interactions promote hormonal balance, which is essential for reproductive success. Positive social behaviors contribute to a more stable environment, reducing stress and encouraging proper hormone signaling, ultimately enhancing the likelihood of successful reproduction in dairy heifers.

MATERNAL BONDING AND REPRODUCTIVE SUCCESS

Early maternal bonding, facilitated by colostrum, improves future reproductive success by fostering emotional and physiological connections. This bonding process supports the calf's ability to cope with stress and enhances its overall well-being [43]. Strong maternal bonds improve hormonal stability and can positively affect fertility by ensuring that the calf's physiological needs are met, fostering better reproductive health.

Behavioral Resilience and Hormonal Stability

Colostrum's impact on behavioral resilience helps maintain hormonal stability, which is essential for reproductive health. Resilient calves experience less stress, leading to better regulation of reproductive hormones [44]. This resilience contributes to improved fertility and reproductive function, as the calf matures into an adult capable of achieving reproductive success with fewer disruptions in hormonal cycles.

Calf Vigor and Reproductive Fitness

Enhanced vigor in colostrum-fed calves promotes reproductive fitness by supporting optimal growth and development [45]. Healthy, vigorous calves are better equipped to cope with stress and thrive in a challenging environment. This increased vitality translates into improved hormonal regulation, better ovarian activity, and enhanced fertility as the heifer matures into adulthood.

STRESS-RELATED HORMONE MODULATION

Colostrum intake helps modulate stress-related hormones, improving reproductive outcomes. By reducing the impact of stress on hormone production, colostrum ensures more consistent and balanced hormonal cycles. This modulation of stress hormones helps prevent disruptions in the reproductive system, leading to better fertility and higher reproductive success in dairy heifers.

Improved Coping Mechanisms and Ovarian Activity

Colostrum strengthens the calf's coping mechanisms, which benefits ovarian activity and overall reproductive health [2]. With better stress management, the calf can maintain more consistent hormonal levels, supporting the proper functioning of the ovaries. This improves the potential for fertility and successful reproduction, as the calf matures and transitions into reproductive adulthood.

Positive Behaviours and Hormonal Pathways

Positive behaviors promoted by colostrum enhance hormonal pathways critical for reproduction [46]. By fostering a healthy emotional state, colostrum ensures that hormone production and regulation occur without interference from excessive stress. These behaviors, in turn, support the optimal development of reproductive organs and function, increasing fertility and reproductive success in the heifer.

Neonatal Stress Reduction and Puberty Onset

Reduced neonatal stress through colostrum intake helps ensure the timely onset of puberty by supporting hormonal balance. Lower stress levels contribute to better development of reproductive organs, including the ovaries and uterus. This early intervention promotes smooth progression through puberty, reducing delays in the onset of estrus and improving reproductive outcomes in dairy heifers.

Social Stability and Estrus Expression

Social stability, influenced by colostrum, plays a significant role in the expression of estrus [47]. A stable social environment reduces stress and fosters better hormonal regulation, facilitating the proper expression of estrus cycles. This stability enhances reproductive health, ensuring that the heifer's estrus behavior aligns with optimal fertility windows, improving reproductive success.

FUTURE DIRECTIONS

Future research should focus on unraveling the specific epigenetic mechanisms through which colostrum influences reproductive health in dairy heifers. A deeper understanding of how bioactive

components, such as hormones, growth factors, and immunoglobulins alter gene expression in reproductive tissues will be crucial. Investigating the role of the gut-reproductive axis in mediating these effects could offer new insights into the complex interactions between early nutrition, gut health, and fertility. Additionally, studies should explore the long-term impacts of colostrum quality on reproductive performance across multiple generations, considering factors, such as ovarian reserve, estrous cycle regulation, and overall fertility. Research aimed at optimizing colostrum collection, storage, and administration techniques could further improve reproductive outcomes in dairy farming. Finally, exploring the potential for epigenetic modifications to be inherited or passed down through generations may open new opportunities for improving herd fertility and productivity in a sustainable manner.

CONCLUSIONS

This study underscores the significant role of colostrum in shaping the reproductive health of dairy heifers through epigenetic programming. The bioactive components of colostrum, including hormones, growth factors, and immunoglobulins, may induce lasting modifications in gene expression that optimize ovarian function, uterine health, and overall fertility. By influencing early developmental processes, colostrum contributes not only to immune protection but also to the long-term reproductive success of heifers. The findings of this study open new avenues for improving fertility and productivity in dairy herds through enhanced colostrum management. Further research is needed to fully elucidate the epigenetic mechanisms at play and their potential to revolutionize reproductive strategies in sustainable dairy farming.

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