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Maternal Immunity "MDA" of Foot-and Mouth Disease Cattle and Buffaloes Calves Unveiled: Dynamics, Decay, Evaluation and Challenges

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Abstract | Foot-and-mouth disease virus (FMDV) serotypes A, O, and SAT2 are endemic in Egypt, this study was designed to evaluate the factors affecting MDA induced from FMD vaccination program from 2019 to 2020. The study results provided important insights into maternal antibody transmission and its effect on FMD immunization responses in cattle and buffalo calves. Species and Lactation Effects: Among the 4 FMD virus serotypes (A.Iran, O, SAT-2 2012, and SAT-2 2017), buffalo calves acquired considerably higher levels of maternal antibody relative to cattle calves at birth. Dam parity markedly affected antibody transfer, with third-lactation (≥3) dams transferring higher antibody levels than first-lactation dams in both species. This impact was most apparent in cattle, where lactation-three dams exhibited antibody ranges close to buffalo dams. For Gender Disparities, Male calves had statistically significant higher maternal antibody titers compared to the females. The effect of gender was less significant than that of species or Dams' lactation. Regarding Antibody Persistence, maternal antibodies exhibited serotype-particular decay patterns during the three-month monitoring period. Antibody levels for serotypes A/Iran and O remained relatively stable from birth to three months age. Nevertheless, SAT-2 lines, specifically SAT-2 2017, exhibited a more substantial decline, with SNT titers diminishing from approximately 1.6 log10 at birth to 1.3 log10 at three months age, indicating an approximate 2-fold reduction/decay. Maternal serum antibody levels at parturition were directly correlated with calf antibody levels. Multiparous cattle (lactation ≥3) had significantly higher dam titers (approximately 2.0 log10) in contrast to primiparous animals (1.4-1.6 log10), explaining the enhanced passive transfer to their offspring. All calf groups, regardless of species or dam parity, maintained at or near protective thresholds (1.5-1.65 log10) antibody tiers across the study. Serotype-specific variations in antibody persistence, particularly the rapid decline of SAT-2 2017 antibodies, suggest that vaccination timing strategies may need to be customized based on circulating virus strains. These findings highlight the need to maintain effective maternal immunization programs to guarantee sufficient passive immunity transmission, particularly in first-lactation dams.

Keywords | FMD, FMDV, Maternal immunity, MDA, SAT2 Serotypes, Immunity, Epidemiology

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INTRODUCTION

Foot-and-mouth disease (FMD) is still a globally significant viral disease afflicting cloven-hoofed livestock, including cattle, Buffaloes, sheep, goats, and pigs. The disease is caused by the foot-and-mouth disease virus, a small, non-enveloped, single-stranded RNA virus belonging to the *Aphthovirus* genus of *Picornaviridae* family (Diab *et al*., 2019; Metwally *et al*., 2023; WOAH, 2024). Marked through its enormously contagious nature and potential to cause rapid, extensive outbreaks, FMD incurs profound economic repercussions through decreased productivity, trade exchange restrictions, and culling measures. While vaccination remains a cornerstone of control strategies, the complexity of FMD epidemiology demands a sound understanding of host immunity, particularly the role of maternal immunity in protecting neonates during vulnerable early age, when the virus caused mortality is high.

Maternal immunity

Maternal Immunity plays a crucial role in protecting young animals from infections like FMD. When a dam is exposed to FMD, her immune system produces antibodies that can be passed on to her offspring through colostrum, the first milk produced after birth. These antibodies provide temporary protection for the young animal while its own immune system is still developing.

There are several methods for evaluating maternal immunity to FMD, including serological tests and challenge by live viruses. Serological tests involve analyzing blood samples from young animals to determine if they have acquired maternal antibodies against FMD. Vaccination, on the other hand, involves administering a vaccine to young animals to stimulate the production of their own antibodies against FMD.

Both methods have their advantages and disadvantages. Serological tests can provide a quick and easy way to evaluate maternal immunity, but they may not always accurately reflect the level of protection provided by maternal antibodies as they measure binding antibodies, which may not always correlate perfectly with functional, virus-neutralizing protection., i.e., the SNT virus strain used, heterologous infections, and high environmental viral load as a good example of maternal immunity failure. Vaccination, while more reliable, can be more time-consuming and expensive. It is important to carefully consider the pros and cons of each method when evaluating maternal immunity to FMD.

This article reviews current knowledge on maternal immunity against foot-and-mouth, with an emphasis on humoral immunity, types of vaccine (oil and alum-based adjuvants), maternal antibody interference, and laboratory strategies, including the serum neutralization check (SNT) used to evaluate immune responses. It also highlights practical implications for vaccination timing and program design, in addition to current research developments and gaps.

Current status of FMD serotypes in Egypt

Egypt is considered a key country in the epidemiology of FMD due to its strategic geographic location, large livestock populations, and transboundary animal moves. Despite vaccination efforts, FMD outbreaks persist across many Egyptian governorates, contributing to its endemic status "FMD" characterized by the co-circulation of a couple of serotypes and lineages. Recent molecular epidemiological studies conducted between 2022 and 2024 highlight the predominance of serotypes A and O, with the SAT2 serotype additionally contributing to outbreaks albeit at decrease frequencies (Diab *et al*., 2019; El-Rhman *et al*., 2020; Wubshet *et al*., 2024).

Serotypes A is the most frequent, accounting for approximately 70% of FMD instances in cattle inside affected regions including Sharkia and Dakahlia. This serotype belongs chiefly to the African topotype, genotype IV, and reveals extensive genetic divergence from the vaccine strains presently deployed in Egypt, in particular within the immunodominant VP1 protein's G-H loop, a critical antigenic site focused by means of neutralizing antibodies. Serotype O, the second maximum frequent, clusters within the East Africa-3 topotype, indicating endemic persistence and capacity for vaccine escape due to collected mutations. The SAT2 serotype, even as much less big, keeps representing a sporadic danger, especially in southern and border regions (El-Rhman *et al*., 2020; Wubshet *et al*., 2024).

Compounding these challenges, Egypt's livestock management practices, characterized by nomadic grazing and animal movements between countries, contribute to the spread and dissemination of various FMDV serotypes, complicating surveillance and management. Furthermore, the excessive density of smallholder farms and the limited biosecurity controls facilitate ongoing viral transmission. Consequently, FMD remains an endemic disease with occasional outbreaks reflecting the continuous viral circulation and suboptimal vaccine matching. The genetic variability and frequent mutations observed in this circulating strain have raised concerns regarding the efficacy of present vaccines derived from older reference strains. Phylogenetic analyses display large genetic and antigenic drift, necessitating the urgent updating of vaccine traces to embody local area isolates. Such genomic adjustments severely impair pass-protection from vaccines, undermining the current immunization applications.

Understanding the serotype dynamics, genetic variety, and vaccine mismatches within Egypt's FMD epidemiological panorama is imperative to optimize vaccination strategies and maternal immunity interventions. This understanding underpins efforts to defend each grown-up animal and neonate vulnerable to infection at some stage in the window previous to active immunization. Research efforts have additionally embraced immunoinformatic tactics for designing multiepitope vaccines tailor-made to circulating strains in Egypt, aiming to triumph over the restrictions posed by using antigenic variability. These modern vaccine design strategies, coupled with better molecular surveillance, are integral to future management packages aiming for powerful ailment mitigation.

Mechanism of maternal immunity in foot-and-mouth disease

In ruminants, along with cattle, sheep, and goats, antibody transfer occurs almost exclusively via colostrum shortly after birth, because the epitheliochorial nature of the placenta prevents in utero transfer. Neonatal intestinal permeability permits efficient absorption of Immunoglobulin G (IgG) at some stage in the primary 24 hours post-parturition, after which gut closure diminishes passive transfer ability. The concentration and antibody quality of the dam's colostrum, stimulated via prior vaccination or herbal exposure, critically influence the resulting levels of maternally derived antibodies (MDAs) within the offspring.

Maternal immunity serves as the first line of protection in neonatal animals in opposition to FMD virus contamination, in general conferred via the passive transfer of immunoglobulins via colostrum. These MDAs recognize FMD viral epitopes, specifically the immunodominant VP1 region, neutralizing circulating viruses and therefore reducing initial susceptibility. The protective effect spans from weeks to months and corresponds with the $T_{1/2}$-lifespan and decline of maternal antibodies. The passive immunity provided through MDAs is particularly crucial during the neonatal period whilst the immune system is immature and not able to successfully overcome multiple immune responses (Bucafusco *et al*., 2019; Kishor *et al*., 2025; Sala *et al*., 2023; Wubshet *et al*., 2024; Yaser *et al*., 2023).

Factors affecting humoral immunity and maternal antibody levels

The magnitude and duration of maternal immunity in offspring hinge on several interacting variables:

- Dam's immune status and vaccination: Dams with high neutralizing antibody titers, achieved through effective vaccination, transfer superior levels of MDAs. Booster doses in pregnant dams can augment colostral antibody concentrations (Akhter *et al*., 2015; Ibrahim *et al*., 2014; Otero *et al*., 2020).
- Vaccine formulation and adjuvant: Different vaccine formulations elicit varying magnitudes and periods of antibody responses in dams, affecting MDAs. Oil-adjuvanted vaccines generally elicit more potent and longer-lasting humoral responses compared with aluminum hydroxide (AlOH) formulations, ensuing in higher maternal antibody tiers. Emerging adjuvants are seeking to refine those responses similarly.
- Species and neonatal physiology: Variability in colostrum uptake, immunoglobulin absorption performance, and decay rates throughout species modifies maternal antibody kinetics.
- Genetic and environmental factors: Host genetics, nutrients, pressure, and concurrent infections can have a great effect on humoral immunity and maternal antibody kinetics. Host genetics play a major role in shaping humoral immune responses in farm animals, with heritability estimates for antibody responses to diverse pathogens starting from low to mild (0.03–0.44), and specific genetic loci associated with immune defense were diagnosed. Nutritional status, especially at some point of being pregnant, seriously affects immune features; for example, selenium supplementation in late gestation enhances humoral immunity at parturition, even as maternal undernutrition can suppress fetal immune gene expression and reduce immune competence in offspring. Environmental pressures, which include management depth and disease exposure, can boom disorder hazard and affect immune system improvement. Environmental stressors during the duration of the periparturient or post-gestation period can compromise colostrum rate and passive transfer of immunity to calves. Concurrent infections or high maternal antibody levels can also modulate humoral immunity in calves, as excessive maternal antibody titers can both enhance passive protection and interact with vaccine responses, affecting the kinetics and specificity of antibody development in younger cattle.
- Colostrum management: Prompt and adequate colostrum ingestion is paramount. The volume, antibody attention, and timing of colostrum ingestion through the neonate drastically affect the level of MDAs. Inadequate consumption results in failure of passive transfer and increased early susceptibility (Edwards, 2015; Kryzer *et al*., 2015; Otero *et al*., 2020; Wubshet *et al*., 2024).

Vaccine types influencing maternal immunity

Oil-Adjuvanted Vaccines: These vaccines employ water-in-oil emulsions, stimulating potent humoral and cellular immune responses in dams through evoking a mixed Th1/Th2 immune response. Consequential high antibody titers in colostrum confer substantial passive immunity to

neonates. However, they may be associated with injection site reactions and require careful formulation.

Aluminum Hydroxide (AlOH)-Based Vaccines: Traditionally used for their safety. AlOH adjuvants primarily stimulate Th2-type humoral immunity but with lower antibody titers and shorter-lived maternal antibody transfer compared to oil-based vaccines (Abd-Ellatieff *et al*., 2023; Emami *et al*., 2022; Sala *et al*., 2023; Wubshet *et al*., 2024).

Maternal antibody interference and vaccination timing

A significant immunological challenge in FMD control concerns the interference of maternally derived antibodies with active vaccination of young stock. Maternal antibodies, while protective, can neutralize vaccine antigens in neonates, impeding active immunization a phenomenon termed maternal antibody interference. This leads to reduced seroconversion and suboptimal immunity. Overcoming this necessitates optimizing vaccination timing, often after maternal antibody titers decline below inhibitory levels, commonly between 3–4 months of age in cattle. Conversely, vaccinating too late leaves an immunity gap when MDAs wane but before the vaccine elicits protection, increasing susceptibility (Akhter *et al*., 2015; Edwards, 2015; Ibrahim *et al*., 2014; Kryzer *et al*., 2015; Otero *et al*., 2020).

Strategies to overcome interference

Careful timing of vaccination is frequently guided by means of monitoring MDA ranges till fall beneath interference thresholds, commonly around three to four months of age in livestock. Use of heterologous or intra-typic vaccines to avoid neutralization by way of maternal antibodies.

Development of novel adjuvants is considered a must in young animal vaccination in order to induce both cellular immunity and humoral responses and potentially overcome maternal antibody neutralization.

Practical considerations: Real-time surveillance of MDA decay is crucial to optimize vaccination schedules, and booster vaccinations are regularly used to enhance immunity as soon as interference wanes (Emami *et al*., 2022; Sala *et al*., 2023; Shin *et al*., 2022).

Laboratory evaluation techniques of humoral immunity in FMD

Assessing humoral immunity, "MDAs and vaccine-induced responses" relies on robust laboratory tests. The most commonly used are:

Serum neutralization test "SNT": It is the gold standard test, which measures the neutralization ability of serum antibodies to FMD viral particles in vitro cell culture. SNT quantifies the ability of serum antibodies to neutralize viral infectivity in cell culture. SNT results correlate closely with protective immunity and are widely used to assess the level and duration of maternal antibodies in calves and vaccination efficacy. This assay requires live virus culture under biosecure conditions and is time-consuming but provides functional information on antibody potency.

Enzyme-linked immunosorbent assay (ELISA)

ELISA: A broadly used, speedy antibody detection technique recognizing FMDV antigens though less unique for neutralization. ELISA is considered sensitive, fast, and amenable to high-throughput screening. ELISA can discover general antibodies; however, it might not distinguish between neutralizing and non-neutralizing antibodies, that can have an impact on safety assessment. Variants of ELISA can detect particular immunoglobulin isotypes or non-structural proteins to distinguish vaccination responses from natural infection (Kishor *et al*., 2025; Yaser *et al*., 2023).

Other techniques (Zaher et al., 2025)

- Virus-Like Particle (VLP) Immunogenicity Assays: Research employs VLPs of FMDV to examine humoral responses in vaccine development.
- Avidity ELISA: Measures antibody binding strength (avidity), providing insights into antibody maturation and quality.
- Molecular and Immunological Assays: Quantitative PCR and cytokine profiling complement antibody assessments to understand immune responses comprehensively.

Aim of the study

This study was designed to evaluate the factors affecting MDA induced from FMD vaccination program from 2019 to 2020.

MATERIALS AND METHODS

Experimental design

The experimental design was established to follow up the maternal immunity in dams' serum at the date of giving birth and correlate with the antibody level found in calves after colostrum intake then follow along the study timeframe.

Animals and vaccine

A farm with a total population of 1500 cattle and 200 buffaloes was included in the study and accepted the experimental design to follow up the maternal immunity and collecting samples from dams and calves at birth

(day 0) then following calves for three months of age. All dams were routinely vaccinated using (TRI-Aphthovac™, MEVAC, Egypt) Inactivated tri-valent foot and mouth disease (FMD) virus serotypes [A (Iran 05), O (Pan-asia 2) and SAT 2]. Animals receive last vaccine dose before start of experiment on August 2019, batch no. 1902210201.

Serum and SNT samples

A total of 315 SNT serum samples were collected over 6 months (65 from Dams, 120 calves were followed up for the full three-months old (serum collected on monthly basis)) till the end of the study.

The collected serum samples were organized as the following:

- Experiment 1 Dam's Antibody Level, Compare the Species factor and lactation effect.
- Experiment 2 Calves Antibody Level, Compare the Species factor and Dam's Lactation.
- Experiment 3 Calves Sex/Gender Factor, Compare the gender factor and Dam's Lactation.
- Experiment 4 MDA of Calves over Time, calves were followed up till 3 months of age.

FMD virus strains

A locally isolated FMD virus strain O pan asia-2; A Iran 05, SAT2/EGY/2012 and SAT2/ 2017 of cattle origin typed and subtyped at the FMD Department, Veterinary Serum and Vaccine Research Institute, Abasia, Cairo. The virus had a titer of $10^{8}TCID_{50}$/ ml in BHK_{21} cell line. These viral strains were stored at – 70 °C till being used.

Tissue culture

Baby hamster kidney cell line ($BHK-_{21}$) was grown using Minimum Essential Medium (MEM) with Earl's salts and 8-10% sterile newborn calf serum according to the technique described by Macpherson and Stocker (Macpherson and Stoker, 1962). The cells were used for virus titration and SNT.

Tissue culture media and solutions

1-Minimum Essential Medium (MEM): Minimum Essential Medium (Modified Eagle's) with Earl's salts and L-glutamine without sodium bicarbonate was obtained from Flow Laboratories, UK. It was used for the growth and maintenance of BHK_{21} cell cultures (Telling and Radlett, 1970).

1. The growth medium was supplemented with 10% newborn calf serum, while the maintenance medium was supplemented with 2% serum and the pH of the maintenance media were adjusted to 7.2 - 7.4
2. Bovine sera: Newborn bovine serum free from viruses and mycoplasma was obtained from Flow Laboratories, UK and used as supplement for cell culture media.
3. Trypsin solution (0.25%): It was supplied as powder by Difco Company and used as dispersing agent for BHK cell cultures.
4. It was prepared according to Lennette (Lennete, 1964), then sterilized by filtration and stored at –20 °C. It was used at concentration of 0.25% solution.
5. Sodium bicarbonate solution: It consists of 4.4 g $NaHCO_3$ dissolved in100 ml double distilled water and sterilized by autoclaving. It was used to adjust the required pH of the cell culture media and solutions.

Titration of FMD virus strains

Virus titration was carried out to determine the 100 $TCID_{50}$ as described by (Reed and Muench, 1938; WOAH, 2022; WRLFMD, 2024).

Serum neutralization test (SNT)

It was performed by the micro titer technique as described by Ferreira (1976) as follow:

1. Serial two-fold dilutions of the tested serum samples were prepared in MEM (Modified Eagle's Medium) in micro titer 96-well tissue culture plate (8 X12).
2. Equal volumes of the diluted tested serum and tittered reference FMD virus (100 $TCID_{50}$/ml), (50ul from each/well) were mixed together and incubated for one hour at 37 °C for neutralization.
3. 150 µl of the growth media (MEM) containing BHK_{21} cells were added to each well.
4. Standard virus, negative serum control and cell control were included in the test.
5. All plates were sealed and incubated at 37°C for 48 hours with daily microscopic examination for the development of CPE.
6. The SN titer of the serum was expressed as the reciprocal of the final serum dilution which neutralized and inhibited the CPE of the used virus according to (Singh *et al.*, 1967).
7. While the serum neutralization index was calculated according to (Reed and Muench, 1938).

Statistical analysis

Statistical analysis was performed using GraphPad Prism 10.0.0 (Software, 2023) SNT titers against different FMD viruses. A one-way ANOVA was performed to assess the statistical significance between group differences for each factor. Followed by Tukey's B test was utilized as the post hoc analysis to compare the serotype immune responses against for each variable.

RESULTS

Experiment 1 Dam's antibody level

Compare the Species factor and lactation effect

Figure 1 illustrates the serum neutralization titers in vaccinated dams on calving day, serving because the

immunological basis for passive antibody transfer. Panel A (FMD-A.Iran) shows dam titers ranging from 1.6 log_{10} (third-lactation buffaloes) to approximately 2.0 log_{10} (third-lactation cattle), with cattle at third-lactation is the significant group. Buffaloes at third-lactation showed notably lower titers (1.6 log_{10}), establishing a clear species advantage for cattle in anti-FMD-A immunity. The hierarchical titers across lactation stages in cattle underscore the progressive immune boosting effect of repeated vaccinations across multiple production cycles. Panel B (FMD-O) reveals greater serotype-specific variability than the FMD-A response, with titers spanning from 1.4 log_{10} (third-lactation buffalo) to 2.1 log_{10} (first-lactation cattle). Notably, first-lactation cattle achieved exceptional titers against the O serotype, suggesting that serotype-specific immune mechanisms may be differentially activated in early versus multiparous cattle. This heterogeneity (p= 0.0002) indicates breed-specific or serotype-strain recognition variations in the vaccine-induced immune response. Panel C (FMD-SAT-2 2012) shows more homogenized responses across groups (1.5–1.9 log_{10} range), yet third-lactation cattle maintained the advantage with the highest titers marked as "A." The slightly elevated baseline titers observed in this panel compared to Panel D suggest a potential temporal effect or vaccine formulation difference between the 2012 and 2017 vaccination protocols. Panel D (FMD-SAT-2 2017) displays the most modest titers observed across all panels (1.5–1.8 log_{10}), with substantially reduced differentiation between groups. The lack of significant statistical difference (p= 0.4805) indicates convergence of immune responses across serotypes and production cycles over time, potentially reflecting vaccine stability, host adaptation, or altered dosing strategies. Notably, dams continuously preserve defensive immunity throughout all serotypes, with multiparous cattle (lactation ≥3) usually demonstrating better titers than primiparous animals. These maternal antibody profiles at once correlate with next calf passive immunity, organizing that vaccination protocol maintenance and parity control are essential for making sure adequate colostral antibody transfer and neonatal protection in opposition to FMD.

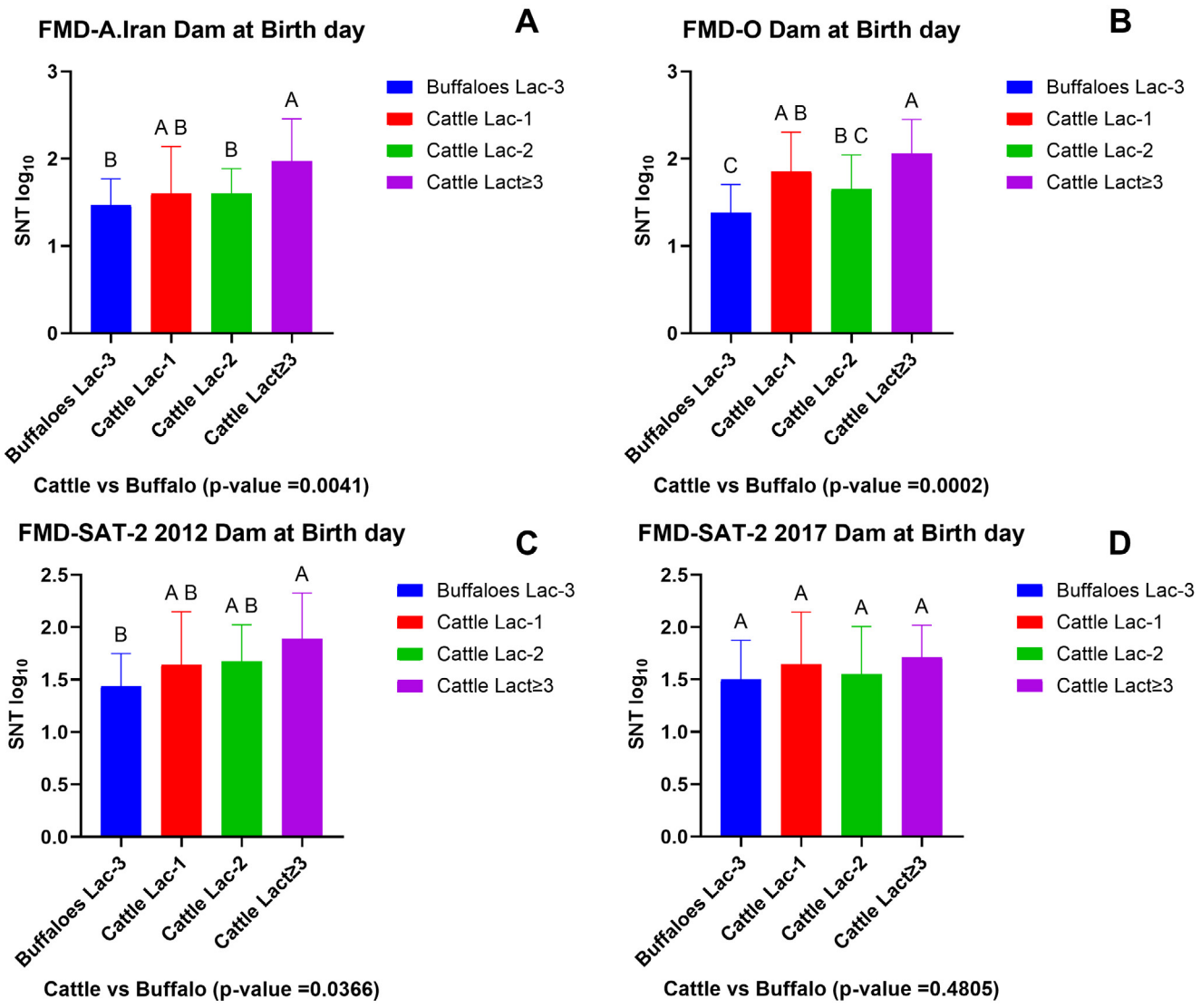

Figure 1: Dam's SNT titers Log_{10} mean titers with different superscript letters are significantly different ($p < 0.05$).

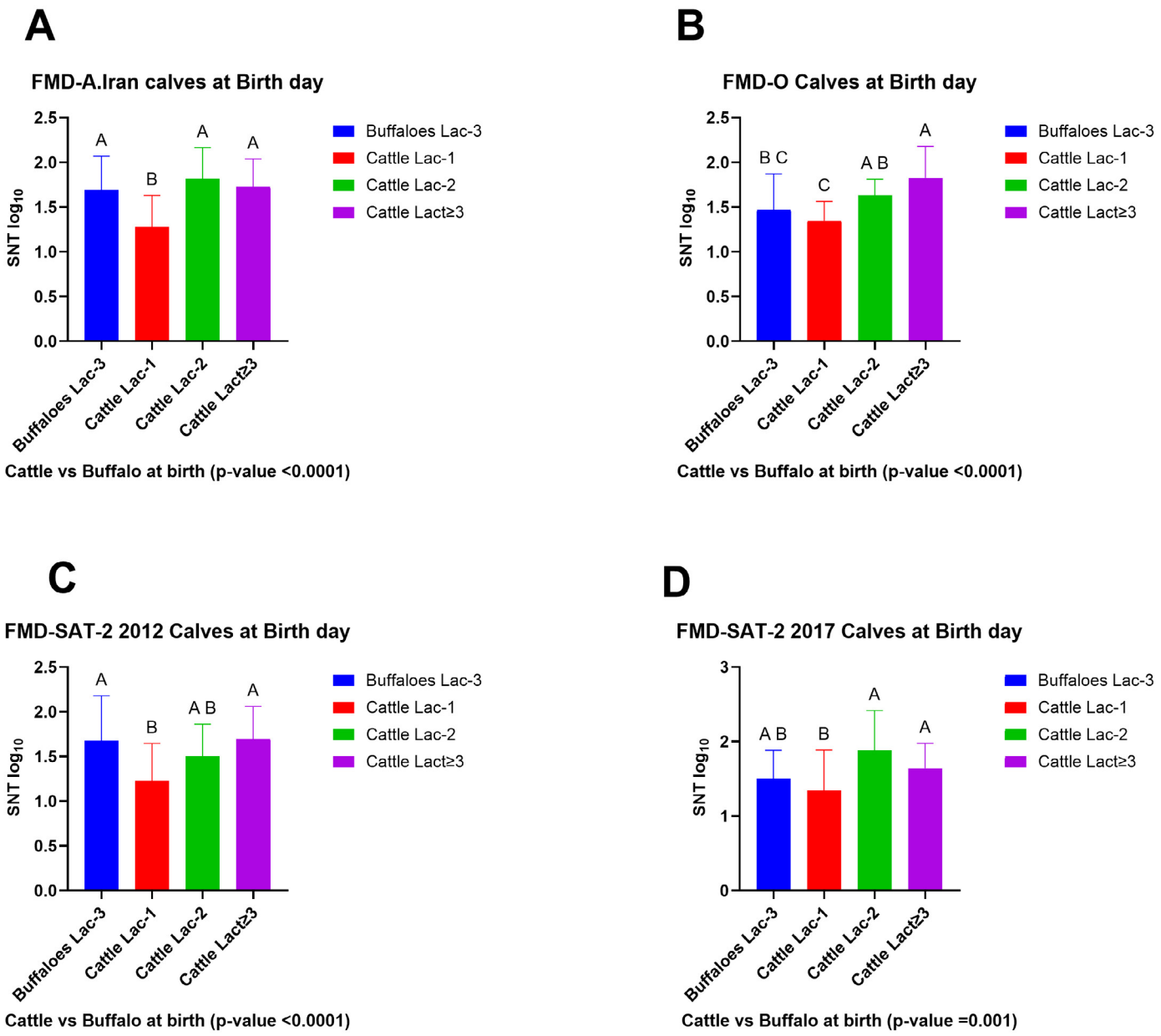

Figure 2: Calves MDA SNT log_{10} vs Dam's lactation mean titers with different superscript letters are significantly different ($p < 0.05$).

Experiment 2 Calves Antibody Level Compare the Species Factor and Dam's Lactation

Figure 2 displays the transfer of maternal derived antibodies (MDA) to calves across four FMD serotypes, stratified by species and maternal lactation parity. Buffalo calves consistently achieved superior SNT titers compared to cattle calves, particularly those from multiparous dams. Panel A (FMD-A.Iran) shows buffalo third-lactation calves at 1.7 log_{10} versus cattle first-lactation calves at 1.25 log_{10}, representing statistically significant differences ($p < 0.0001$). Similar patterns emerge across all panels: Panels B, C, and D reveal buffalo and high-parity cattle calves acquiring titers of 1.5–2.0 log_{10}, while primiparous cattle calves demonstrate notably lower passive protection. This phenomenon underscores that colostral antibody quality and quantity are critically dependent on maternal immune status, with profound implications for neonatal disease susceptibility during the vulnerable early life period. These consequences emphasize that colostral antibody transfer is optimized in buffaloes and multiparous livestock, specifically crucial for neonatal sickness protection all through the crucial early life period.

Experiment 3 Calves Antibody Level Compare Sex/Gender Factor

Figure 3 shows serum neutralization test (SNT) titers comparing male and female calves throughout the four FMD serotypes, revealing sex-specific and species-dependent patterns in maternal antibody inheritance. Panel A (FMD-A.Iran) demonstrates that male buffalo calves from third-lactation dams achieved substantially higher titers (approximately 1.8 log_{10}) compared to male

cattle calves from primiparous dams (1.3 log_{10}), with statistical significance ($p < 0.0001$). Panels B through D show consistent patterns with FMD-O and SAT-2 serotypes, where buffalo-derived calves maintained superior antibody levels regardless of sex. Notably, Panels C and D reveal variable sex effects within specific groups, with certain female calves exhibiting comparable or marginally superior titers relative to male counterparts from identical dam groups. This nuanced sex-based heterogeneity, combined with the dominant influence of maternal lactation history and species, suggests that while both biological and immunological factors govern passive antibody transfer, maternal immune status fundamentally determines neonatal protection levels across FMD serotypes. Statistical importance is indicated by using letter superscripts (A, B, C) representing Tukey's post hoc test results. The overall pattern indicates that both the level of maternal immunity (reflected in the dam's lactation number) and animal species significantly influence passive antibody transfer to calves, with buffaloes generally acquire higher maternal immune levels as compared to cattle (Bucafusco *et al.*, 2019).

Figure 4 illustrates the critical temporal decline of maternal derived antibodies (MDA) across a three-month observation period, revealing serotype-dependent decay kinetics with significant clinical implications for vaccination timing. Panel A (FMD-A.Iran) demonstrates robust MDA persistence, remaining relatively stable from birth (1.7 log_{10}) through three months (averaging 1.8 log_{10}), suggesting extended protective capacity against this serotype. Panel B (FMD-O) similarly exhibits minimal titer reduction over the observation period. Conversely, Panels C and D reveal markedly accelerated MDA decay

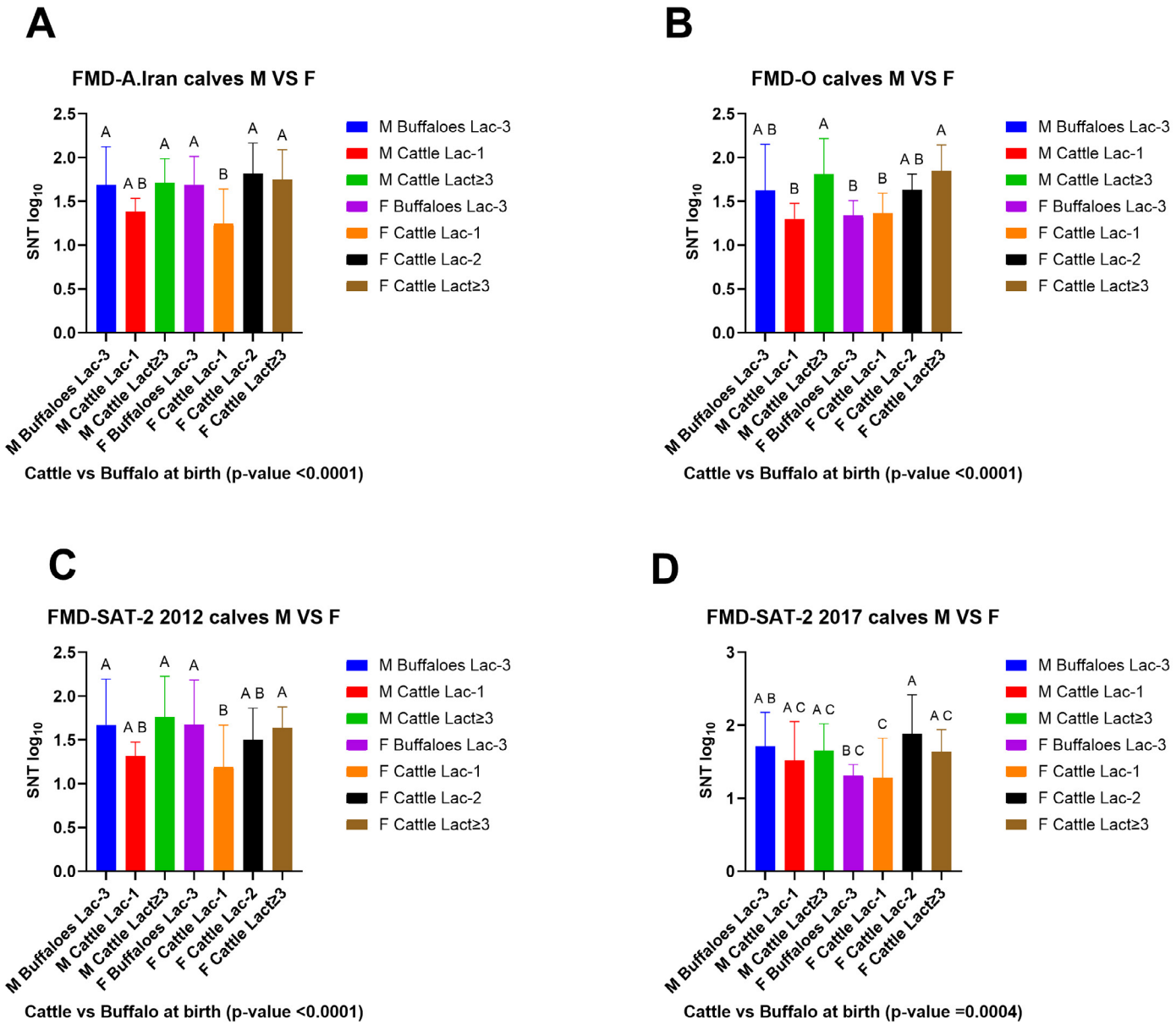

Figure 3: Calves MDA SNT log_{10} vs gender factor mean titers with different superscript letters are significantly different ($p<0.05$).

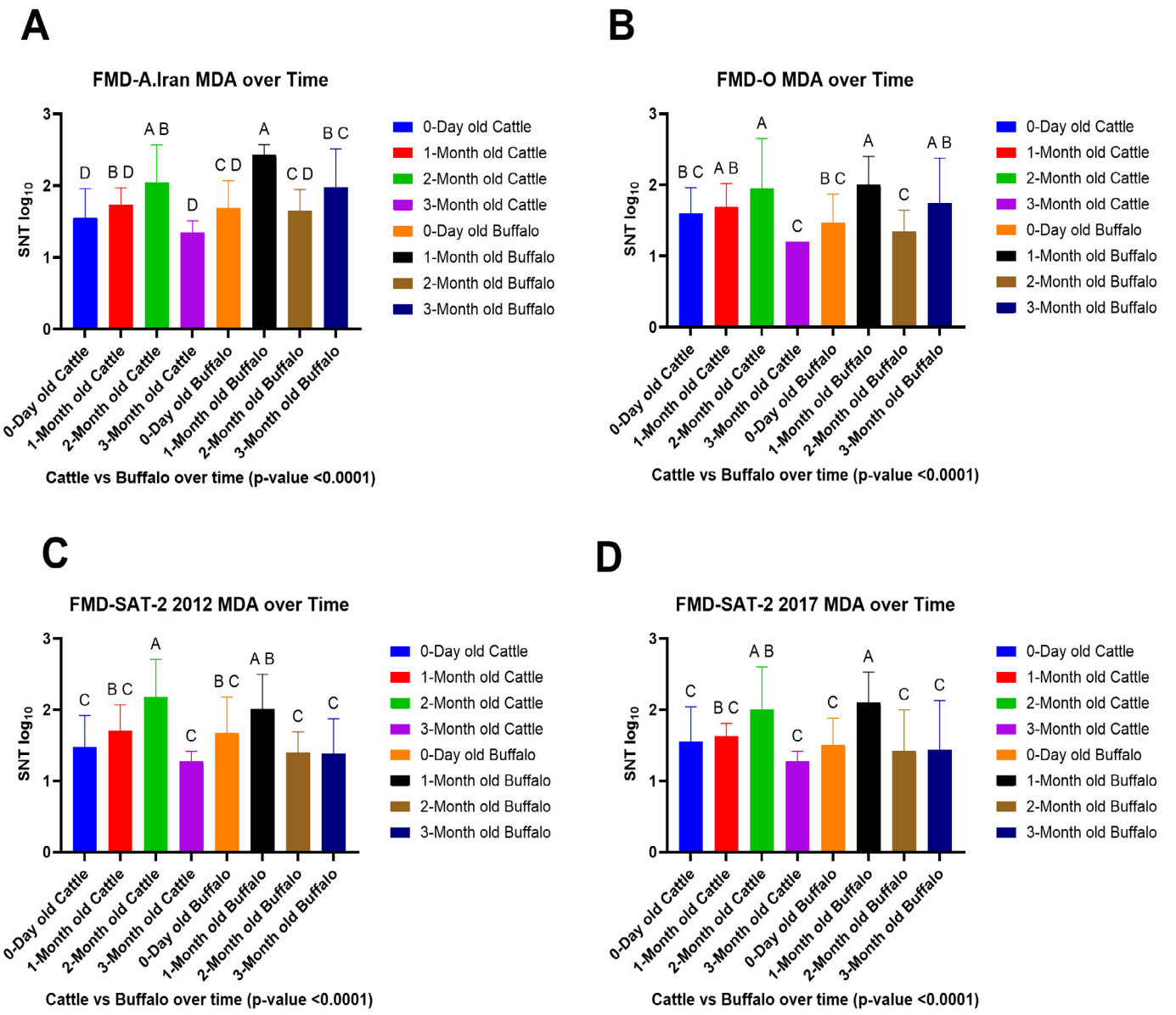

Figure 4: Calves MDA SNT log_{10} over time.

for SAT-2 serotypes, with 2012 and 2017 strains both declining from approximately 1.6 log_{10} at birth to 1.3 log_{10} by three months. Buffalo calves consistently maintain higher titers throughout all timepoints compared to cattle. This differential serotype-specific antibody decay pattern highlights a critical vulnerability window: calves lose protective immunity against SAT-2 viruses substantially earlier than against FMD-A and Pan-Asia-2 serotypes, necessitating serotype-tailored vaccination protocols to optimize timing and prevent neonatal disease susceptibility during the protection-free interval.

DISCUSSION

Foot-and-mouth disease (FMD) is a highly contagious viral disease that affects cloven-hoofed animals, including livestock such as cattle, sheep, and pigs. The disease is characterized by fever, blisters on the tongue, lips, and feet, and can lead to severe economic losses for agricultural production systems (Yang *et al*., 2014). In Egypt, the epidemiology of foot-and-mouth disease outbreaks has been a significant concern for the livestock industry, with recurring outbreaks reported over the past two decades (Dahiya *et al*., 2020; Diab *et al*., 2019).

These maternal antibody SNT profiles directly establish the colostral antibody reservoir available for neonatal passive immunization. Multiparous cattle, particularly those at third-lactation status, provide superior passive protection due to consistently higher titers. The serotype-specific variations observed particularly the FMD-O response advantage in primiparous cattle indicate that maternal age and previous antigenic exposure differentially influence antibody transfer by serotype, necessitating nuanced vaccination timing strategies to optimize colostral quality across all serotypes.

Buffalo calves display higher maternal antibody degrees compared to cattle calves across all FMD serotypes. It is strongly supported by multiple studies inspecting species-specific immune responses in ruminants. Research on virological and immunological research of FMD type SAT2 in clearly infected and vaccinated buffalo cows verified that buffaloes own superior antibody production capacity, with vaccinated buffalo cows capable of provide calves with high degrees of maternally derived antibodies via colostrum that could defend newborns for at the least 14 weeks post-partum. This superior antibody transfer in buffaloes in comparison to cattle has been attributed to variations in placental shape, colostrum composition, and ordinary immune competence among species. The heterogeneity study in antibody responses to FMD primo-vaccination discovered extensive breed-related differences, with Jersey cattle displaying significantly lower antibody responses ($p<0.05$) compared to Holstein cattle throughout all three vaccine traces tested. This genetic-borne version in immune response shows that species and breed differences essentially impact each maternal antibody production and passive transfer efficiency. Furthermore, research on immune mobile transfer via colostrum confirmed that passive transfer of maternal antibodies from colostrum became equally green irrespective of the presence or absence of maternal immune cells, however species-unique factors still stimulated absolutely the antibody portions transferred (Bucafusco *et al*., 2019; Di Giacomo *et al*., 2015; Ibrahim *et al*., 2014).

However, a few studies suggest that the apparent species superiority in antibody transfer may be confounded through control factors in preference to inherent organic differences. An observation on maternal antibody persistence in calves determined that once cattle from well-managed farms with everyday vaccination protocols were in comparison to buffaloes beneath comparable situations, the variations in maternal antibody stages were much less mentioned than to start with found. Research on colostrum pleasant determinants indicated that factors which includes dam parity, time of first colostrum feeding, colostrum quantity ate up, and maternal vaccination timing had extra widespread affects on calf antibody ranges than species alone. Additionally, research examining breed variations within cattle species showed sizable intra-species variation that every now and then handed inter-species variation, suggesting that genetic factors within species may be as essential as species class itself. The look at on immune cells transferred by means of colostrum confirmed that when colostrum preparations had been standardized for antibody content, the kinetics of antibody waning in calves were practically equal regardless of maternal species, indicating that the number one distinction lies in initial antibody concentration instead of essential variations in antibody half-existence or function (Akhter *et al*., 2015; Bucafusco *et al*., 2019; Di Giacomo *et al*., 2015; Ibrahim *et al*., 2014).

The results showed that multiparous dams (lactation ≥3) provide appreciably higher antibody tiers to their offspring as compared to primiparous dams is robustly supported by more than one unbiased research. Research on buffalo calves born to vaccinated dams showed that antibody titers in colostrum and serum extended gradually with dam parity, with 0.33 lactation dams generating colostrum with antibody titers approximately 1.3-1.5 fold higher than first-lactation dams. This parity impact has been attributed to cumulative immune reminiscence development via repeated vaccination cycles and natural publicity to pathogens over a couple of pregnancies. The immune cellular transfer study validated that even as maternal immune cells themselves may not considerably regulate vaccine responses, the antibody quantity transferred which will increase with parity without delay correlates with the degree of interference determined in calf vaccination responses. Studies on persistence of maternally derived antibodies found out that calves born to multiparous dams maintained protective antibody degrees (PI fee ≥50%) for prolonged durations in comparison to calves from primiparous dams, with differences of 2-3 weeks in antibody persistence period. Mechanistic research suggest this parity impact consequences from innovative increases in memory B mobile populations and improved germinal center responses with each next pregnancy and vaccination, leading to better exceptional antibodies with stepped forward avidity and broader go-reactivity (Akhter *et al*., 2015; Bucafusco *et al*., 2019; Di Giacomo *et al*., 2015; Ibrahim *et al*., 2014).

Conversely, a few studies indicate the parity effect can be overestimated due to confounding elements, mainly in discipline research in which older animals have inherently received more vaccinations simply due to age rather than parity. A comprehensive look at on heterogeneity in antibody responses found that when vaccination history changed into cautiously controlled ensuring animals received same numbers and timing of vaccinations irrespective of parity the parity impact was appreciably decreased, even though still statistically sizable. Research on FMD vaccine evaluation in Iranian cattle farms indicated that the timing of vaccination relative to parturition had a more significant impact on colostral antibody tiers than parity variety alone, with vaccinations administered 4-6 weeks earlier than calving producing premiere antibody transfer no matter parity. Studies on maternal antibody interference in human vaccines provide parallel proof that maternal immune status on the time of delivery, as opposed to cumulative pregnancy number, is the number one determinant of antibody transfer efficiency. Additionally, research analyzing dietary popularity and

standard herd health counseled that the plain parity impact would possibly partly mirror better body situation and health popularity of multiparous animals in nicely-managed herds, as nutritionally harassed primiparous animals showed disproportionately decreased antibody manufacturing in comparison to well-nourished opposite numbers. Some studies have also cited that extraordinarily high parity (>6 lactations) may additionally really result in decreased antibody transfer because of age-associated immune senescence and decreased colostrum satisfactory (Di Giacomo *et al*., 2015; Edwards, 2015; Emami *et al*., 2022; Ibrahim *et al*., 2015).

Male calves tended to have slightly higher maternal antibody levels than female calves, though the difference was modest; this finds support in several immunological studies examining intercourse-primarily based differences in passive immunity. Research on Human and toddler immune responses documented that male infants born to vaccinated mothers validated marginally better wire blood antibody titers as compared to woman toddlers, probably due to differences in placental antibody transfer efficiency influenced with the aid of intercourse hormones. A examine on measles vaccination said that women had decrease ranges of maternal measles antibodies and better threat of subclinical contamination before the age of vaccination in comparison to boys, suggesting intercourse-particular variations in maternal antibody persistence or preliminary transfer. However, in the context of FMD vaccination responses, those gender variations in maternally derived antibodies did not translate to extensive differences in vaccine-triggered immune responses whilst assessed by way of ELISA, SNT, or cell immunity assays. Studies on heterogeneity in antibody responses to FMD vaccination observed no substantial affiliation among calf intercourse and publish-vaccination antibody titers when genetic (sire) and environmental (farm) elements were properly managed. The lack of a major gender effect on vaccine responses, notwithstanding modest variations in maternal antibody levels, indicates that the variety of maternal antibody variant due to intercourse is inadequate to significantly impact vaccine immunogenicity within the traditional vaccination schedules used (Di Giacomo *et al*., 2015; Edwards, 2015; Le *et al*., 2022; Otero *et al*., 2020).

However, conflicting evidence exists regarding intercourse-primarily based differences in each maternal antibody transfer and vaccine responses, with a few studies finding no full-size intercourse differences at the same time as others report contrary styles. Research on rotavirus vaccine efficacy validated that the intercourse of the infant did now not considerably correlate with maternal antibody ranges or vaccine immunogenicity in large-scale scientific trials performed in low- and center-profits nations. Studies analyzing immune gadget improvement in cattle revealed that whilst intercourse hormones have an impact on immune cell populations and cytokine profiles, these differences become more reported after sexual maturity in preference to in neonatal calves at the everyday age of first vaccination. A comprehensive overview of maternal antibody interference throughout multiple vaccine structures found inconsistent proof for sex-unique outcomes, with most properly-managed studies failing to stumble on good sized intercourse variations when sample sizes have been ok and confounding variables had been nicely adjusted. Some studies has even advised that apparent sex differences in antibody degrees or vaccine responses might mirror sampling bias, as male and femalecalves can be managed otherwise in manufacturing systems, with differential retention guidelines affecting which animals remain available for sampling at later timepoints. Additionally, research on maternal immunity transfer in other species have shown that whilst fetal intercourse can impact placental development and feature, the net impact on antibody transfer is notably variable and depending on maternal elements consisting of parity, vitamins, and normal fitness status, which may additionally overshadow any intrinsic sex-based totally differences (Akhter *et al*., 2015; Brun *et al*., 1976; Bucafusco *et al*., 2019; Edwards, 2015; Ibrahim *et al*., 2014; Kishor *et al*., 2025; Madhanmohan *et al*., 2009; Otero *et al*., 2020; Shin *et al*., 2022).

Maternal antibodies persist at defensive levels for approximately 14-23 weeks put up-beginning, with serotype-unique version in decay prices, is drastically documented throughout a couple of FMD vaccine research. Research on maternally derived antibodies persistence in calves proven that protective degrees (PI fee ≥50%) have been maintained till 22-23 weeks of age, declining below shielding thresholds with the aid of 27-28 weeks (about 6 months), regular together with your experimental timeline. Studies calculating antibody 1/2-existence confirmed that FMD-precise maternal IgG antibodies have expected half of-lives starting from 15.35±2.5 days for IgM to 20.43±6.4 days for IgG2, with IgG1 and overall/neutralizing antibodies showing intermediate values of 16-18 days. This differential persistence among immunoglobulin isotypes explains the slow transition from maternal to lively immunity and informs most efficient vaccination timing strategies. Research on buffalo calves born to vaccinated dams showed that antibodies in calves' sera declined progressively, with the highest maternal antibody titers recorded at 1-2 days submit-partum (following colostrum consumption), keeping protective ranges (1.5-1.6 $\log_{10}$) (WOAH, 2022) for 14-16 weeks earlier than losing beneath shielding thresholds. Studies examining antibody kinetics demonstrated that the price of maternal antibody decline follows first-order kinetics and can be

as it should be modeled the use of exponential decay functions, permitting prediction of while calves end up at risk of infection or attentive to vaccination (Akhter *et al*., 2015; Bucafusco *et al*., 2019; Ibrahim *et al*., 2014).

Faster decay of SAT-2 2017 MDA is likely multifactorial. SAT-2 strains circulating in Egypt, Libya, and Sudan show marked antigenic and genetic diversity, with evidence of recent introductions and vaccine–field strain mismatch, which can reduce affinity and longevity of neutralizing antibodies and accelerate functional waning. Compared with serotypes O and A, SAT-2 responses in buffalo and cattle often peak later and fall earlier, especially after oil-adjuvanted monovalent vaccination. This suggests that the specific SAT-2 2017 antigen, rather than adjuvant alone, elicits a shorter-lived B-cell response, possibly compounded by prior natural SAT-2 exposure in dams that generated lower-quality, rapidly catabolized maternal IgG (Akhter *et al*., 2015; Ibrahim *et al*., 2014).

However, the staying power of maternal antibodies suggests large individual version that demanding situations the establishment of regularly occurring vaccination timing pointers. Research on heterogeneity in immune responses revealed that even inside single farms with standardized control, character calves confirmed coefficient of variant exceeding 30% in antibody decay fees, making it hard to perceive a single most advantageous vaccination age that suits all animals. A have a look at on assessment of FMD vaccine effectiveness in Iranian cattle tested that factors along with colostrum consumption timing and volume, passive transfer efficiency, and male or femalemetabolic rates appreciably influence how long maternal antibodies persist, with some calves losing defensive immunity by using 12 weeks at the same time as others maintained it beyond 24 weeks. Research on maternal antibody interference with vaccine responses confirmed that even enormously low, technically "sub-shielding" maternal antibody tiers can still intrude with active immune responses to vaccination, suggesting that waiting for complete maternal antibody disappearance may be necessary for surest vaccine efficacy but will increase the window of susceptibility to contamination. Human Studies analyzing the effect of breast milk antibodies on oral vaccine responses proven that continuous antibody exposure thru nursing can extend the purposeful persistence of maternal immunity beyond what serum antibody measurements on my own might expect, specifically for mucosal pathogens like certain FMD virus strains. Additionally, studies on vaccine formula influences found out that exclusive vaccine traces and adjuvant structures may engage differently with residual maternal antibodies, with some modern-day oil-adjuvanted vaccines able to overcoming low-to-slight maternal antibody degrees more efficiently than conventional aqueous formulations, complicating the determination of most beneficial vaccination timing (Akhter *et al*., 2015; Di Giacomo *et al*., 2015; Edwards, 2015; Emami *et al*., 2022; Ibrahim *et al*., 2014; Otero *et al*., 2020).

In conclusion, buffalo and multiparous cattle consistently show higher SNT titers at calving and at birth of calves than primiparous cattle, confirming efficient colostral transfer and parity-dependent. By gender, there was male–female differences, suggesting that species and dam lactation status are stronger determinants than calf sex. Longitudinal MDA study reveals that MDAs against FMD-A Iran and FMD-O are relatively stable over the first three months, whereas SAT-2 2012 and 2017, particularly the 2017 strain, displays a faster decline, indicating serotype-specific persistence and a potentially narrower window of passive protection. Overall, the data strongly support that buffalo and high-parity cattle are key sources of effective MDA, while SAT-2 MDAs wane earliest, indicating timing need of primary FMD vaccination in young stock.

Practical implications, research advances, and research gaps

Advancements in understanding maternal immunity against FMD have revealed:

- Knowledge on maternal immunity and its determinants drives the vaccination techniques, emphasizing dam vaccination, colostrum management, timing for neonatal vaccination, and vaccine component/strain improvements. Research focuses on the direction of novel adjuvants, epitope-based vaccines, and incorporation of molecular surveillance to overcome current challenges.
- The modulation of antigenic specificity with the aid of maternal antibodies, influencing next humoral responses in offspring. Development of novel adjuvanted vaccines that elicit stronger and longer-lasting immune responses, probably overcoming maternal antibody interference. Insights into molecular immune evasion mechanisms with the aid of FMDV and host immune responses, guiding vaccine design.

However, challenges remain including

Precisely predicting MDA decay kinetics under field conditions across different species and environments. Designing vaccines that elicit broadly protective immunity without compromising safety or incurring high costs. Balancing vaccination timing and coverage to prevent immunological gaps in young stock. Standardizing serological assays to improve comparability and interpretation of immune status across studies and regions.

Study limitations

There was limited number of animals used in this study due to farm owners' agreement to the study. Also, farmers not always follow the Dam's booster vaccination 4-6 weeks before calving recommendation. Finally, some Dams and calves were sold out before finishing the experimental protocol.

Future work

It is recommended to study the interaction between maternal immunity MDA versus vaccination time and its effect on the antibody response also studying the difference between cattle's and buffaloes' humeral immune response.

CONCLUSIONS AND RECOMMENDATIONS

In conclusion, Maternal immunity plays a crucial role in the early defense against foot-and-mouth disease virus infection in neonates through colostrum. The effectiveness and length of this immunity depend on the dam's vaccination status, vaccine method, and colostrum management, amongst other elements. Meanwhile, maternal antibodies have a key role in protection; they also can interfere with the active immunization of younger animals,demanding cautious timing of vaccination to obtain optimal vaccine efficacy. Advances in vaccine adjuvants and immunomodulators promote immunogenicity and deal with maternal antibody interference in the future. Field surveillance is crucial to refine maternal immunity understanding and optimizing global control of FMD.

Ethics approval

The ethical and research committee at the Faculty of Veterinary Medicine, Cairo University, approved the study protocol under reference number (CU-II-F-30-20).

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NOVELTY STATEMENT

This a recent study Correlate the difference in foot-and-mouth disease vaccine immune response between cattle and buffaloes with the level of MDA acquired by calves after colostrum intake.

AUTHOR'S CONTRIBUTION

ED, AAF, SAA, and MME designed the study. ED, MAE, and MHK performed laboratory and statistical analyses. Each author has made an equal contribution in offering their technical expertise and insights to develop this article.

Generative AI and AI-assisted technology statement

We declare that AI assisted tools had been used mainly to improve language clarity of the manuscript, while all interpretations, conclusions, and scientific content were designed, created and verified by the authors.

Conflict of interest

The authors have declared no conflict of interest.

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