J. Dairy Sci. 109:824–840
https://doi.org/10.3168/jds.2025-26908
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Associations between prepartum dam metabolism, colostrum, and heifer calf development

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ABSTRACT

The aims of this study were to (1) investigate the relationships between prepartum body condition, metabolic status, dam milk variables, and colostrum yield and its immunological and nutritional components; (2) investigate the relationships between colostrum variables of dams and female offspring's growth and metabolism from birth to weaning, from weaning to calving, and during the first 100 DIM; and (3) evaluate the correlation between dam colostrum variables in dams and those of their offspring after their first calving. Data and colostrum samples originated from a previous experiment that was designed to evaluate the effect of voluntary waiting period on health of dams and female offspring. In the current study, Holstein-Friesian dairy dams (n = 62) that calved female offspring with different calving interval (CInt) were included. The available prepartum variables of those dams included BW, BCS, milk yield, DMI, and energy balance (EB), and blood metabolites were assessed before calving. After calving, colostrum variables were measured, including yield, Brix value, protein, growth factors, and antibodies. Body weight and blood metabolites of female offspring (n = 62) from those dams were monitored across 3 stages: calf from birth to weaning, heifer from weaning to calving, and lactating offspring during first 100 DIM, and colostrum variables after their first calving. To investigate relationships between prepartum dam condition, dam colostrum, and female offspring development from birth to weaning and until lactation, each dam variable or colostrum variable were included separately in a regression model, with fixed effects of dam's CInt, parity, time, and their 2-way interactions, repeated over time. Higher BCS before calving was related to lower lactoferrin concentration in colostrum. Greater prepartum EB was related to higher IgM concentration in colostrum, which was related to higher keyhole limpet hemocyanin (KLH)-IgM and IgG levels in offspring plasma from birth until lactation. Greater milk yield in the last week before dry-off was related to higher concentrations of insulin-like growth factor-I (IGF-I) and transforming growth factor-β2 (TGF-β2) in dam colostrum. Higher concentrations of IGF-I and TGF-β2 in colostrum were related to higher plasma nonesterified fatty acid concentrations of calves from birth to weaning, as well as higher milk lactose content during lactation. The positive relationships between KLH-IgG titers in colostrum and offspring plasma remained consistent from birth until lactation. Additionally, higher colostrum yield in dams was associated with higher colostrum yield in female offspring. In conclusion, dairy dam DMI and EB were positively related to natural antibody levels in colostrum, which, in turn, were positively related to natural antibody levels in offspring plasma from birth to weaning and through lactation. Overall, colostrum, influenced by prepartum dam conditions, is related to offspring long-term immunity.

Key words: transgenerational effects, immunity, growth factors, offspring

INTRODUCTION

Bovine colostrum is an important factor for growth and development of calves (Costa et al., 2023). It is the first postcalving secretion from the mammary gland, consisting of various nutritional and immunological components, including Ig. Bovine colostrum contains 3 major classes of Ig: IgG, IgM, and IgA (Korhonen et al., 2000). Pritchett et al. (1994) recommended that colostrum with more than 50 g/L of IgG was considered as high quality. A subset of Ig are natural antibodies (**NAb**), which are defined as antibodies present in healthy animals without intentional antigenic stimulation (Baumgarth et al., 2005) and are considered to belong to the humoral part of the innate immune system (Ochsenbein et al., 1999; Reyneveld et al., 2020). In addition to its role as a supplier of

Received May 9, 2025.
Accepted October 7, 2025.
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The list of standard abbreviations for JDS is available at adsa.org/jds-abbreviations-25. Nonstandard abbreviations are available in the Notes.

Ig, colostrum is also rich in nutrients and biologically active substances such as proteins, lactoferrin, and growth factors (Batista da Silva Galdino et al., 2021), such as IGF and transforming growth factors (**TGF**).

Colostrogenesis starts 3 to 4 wk before parturition (Baumrucker and Bruckmaier, 2014), and therefore prepartum conditions of dairy cows could influence the yield and composition of colostrum. Multiple cow factors have been associated with colostrum yield and composition, including parity, dry period length, metabolic status, body condition of dairy cows during gestation, calving season, as well as colostrum collection moment and storage (Gulliksen et al., 2008; Kessler et al., 2020). Numerous reports have shown that bovine colostrum from multiparous cows has greater Ig and IGF-I content than colostrum from primiparous cows (Costa et al., 2021; Cordero-Solorzano et al., 2022; Tortadès et al., 2023). A short dry period resulted in lower yield and lower fat content in colostrum (Javani et al., 2023). In contrast, Mayasari et al. (2015) did not find any effects of a short dry period on colostrum yield or components. Calving in winter or autumn may result in lower colostrum yield but higher Ig content than calving in spring and summer (Conneely et al., 2013; Dunn et al., 2017). Greater prepartum nonesterified fatty acids (**NEFA**) and BHB concentrations in serum were associated with higher colostrum yield (Westhoff et al., 2023), and lower prepartum glucose concentration in serum was associated with lower IgG concentration in colostrum (Rossi et al., 2023). An inverse relationship between colostrum yield and IgG concentration has been attributed to a dilution effect, where increased colostrum volume lowers IgG concentration (Conneely et al., 2013).

Newborn calves need colostrum to obtain Ig because they are agammaglobulinemic at birth, due to the inability of maternal Ig to pass the bovine placenta in utero (Straub and Matthaeus, 1978; Vogels et al., 2013; Ahmann et al., 2021). The largest proportion of bovine colostrum growth factors are IGF, which stimulate tissue, body growth, and development of newborn calves (Georgiev, 2008). Another important growth factor is TGF-β, involved in the proliferation of intestinal epithelial cells (Koyama and Podolsky, 1989; Blum, 2006). TGF-β contributes to maintenance of gut barrier integrity by balancing regulatory and inflammatory processes and shaping mucosal dynamics (Playford et al., 2000; Konkel and Chen, 2011). Lactoferrin, a multifunctional iron binding glycoprotein, plays an important role in immune regulation and defense against bacteria, fungi, and viruses (Berlutti et al., 2011).

Several studies revealed the effects of maternal lactation or stress during gestation on offspring production and longevity (González-Recio et al., 2012; Weller et al., 2021). A previous study (Wang et al., 2025) showed that dam metabolites and milk performance during different stages of gestation were related to the metabolism and body condition of offspring during early life and adult life. The aim of the current study was to get more insight into the role of colostrum as an intermediate factor, on long-term relationships between dam-calf pairs, examining the relationships between prepartum conditions, colostrum yield and its immunological and nutritional components, and female offspring (**FO**) development. The current study will first investigate the relationship between prepartum body condition, metabolic status, milk variables of dams, and colostrum yield and its immunological and nutritional components. The second objective was to investigate the relationship between colostrum variables of dams and FO's growth and metabolism from birth to weaning, from weaning to calving, and during the first 100 DIM. Moreover, the third objective was to evaluate the correlation between colostrum variables of dams and those of their offspring after their first calving. It can be hypothesized that changes in colostrum yield and quality related to prepartum dam variables influence growth and metabolism of offspring.

MATERIALS AND METHODS

Animals and Experimental Design

The experimental protocol was approved by the Institutional Animal Care and Use Committee at Wageningen University & Research (the Netherlands), with approval number AVD401002016653. Data and colostrum samples originated from an experiment that was designed to evaluate the effect of voluntary waiting period (**VWP**) on health of dams and FO. The experimental design (Figure 1), sample size calculation, and treatments of VWP and management of dams were described earlier by Burgers et al. (2021) and Wang et al. (2024). In brief, Holstein-Friesian dairy dams (n = 154; 41 primiparous, 113 multiparous) were blocked based on parity, milk production in the previous lactation (multiparous cows) or expected milk production (primiparous cows), and SCC, and then randomly allocated to VWP treatments. Of the enrolled 154 dams in the previous experiment, 127 gave birth to a second calf within the experiment. Of these 127 dams, 62 were female calves that were included in the current study, whereas 65 were male calves or twins, which were excluded. For the current study, those 62 dams with female calves were followed for milk production, and specifically from 2 wk before expected calving until calving for feed intake, BW, and BCS and sampling of blood. Two calving events were recorded: The first calving occurred before the VWP treatment (referred to as calving 1), and the second calving occurred after the completion of VWP treatment (referred to as calving 2). Female off-

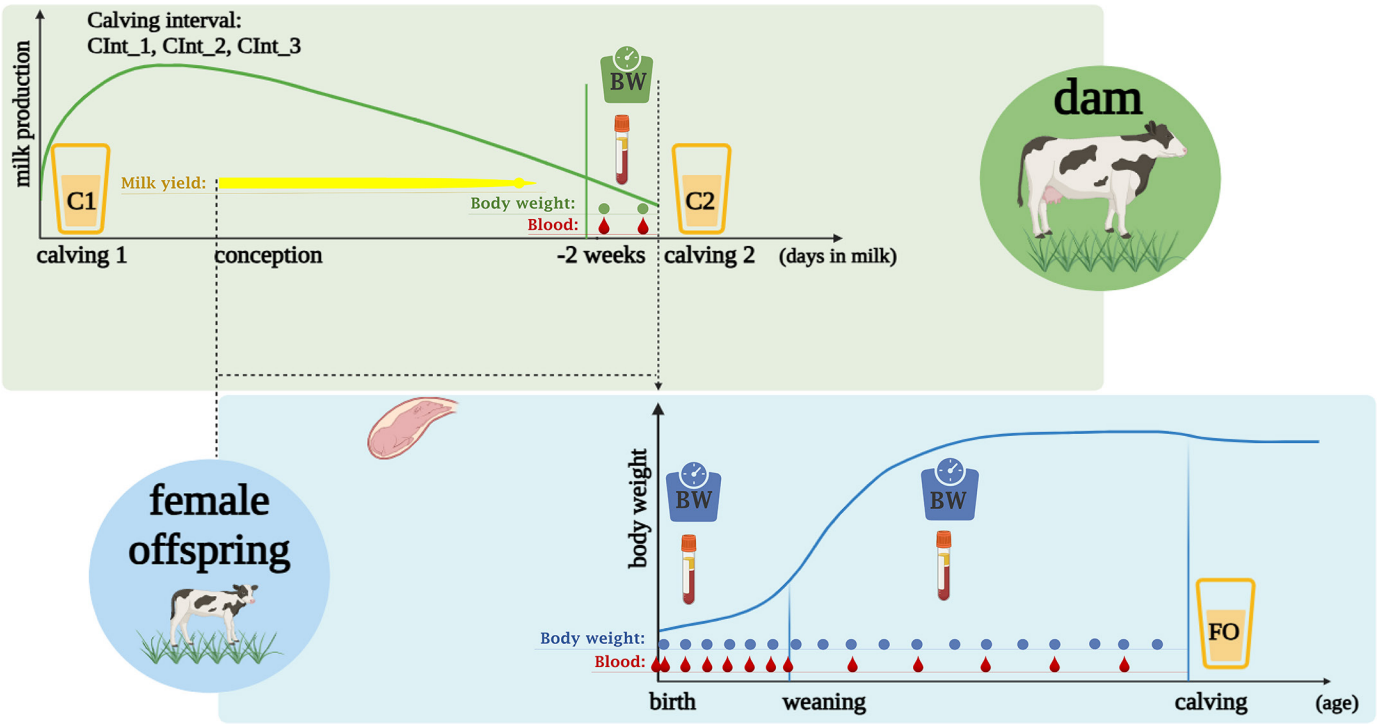

Figure 1. Conceptual overview of the experimental design with different moments of sampling. CInt = calving interval. C1 = colostrum from dam calving 1; calving 1 means the calving before VWP treatment. C2 = colostrum from dam calving 2; calving 2 means the calving after VWP treatment. FO = female offspring. The blood droplet indicates blood sampling: for dams, weekly during last 2 wk before calving 2; for FO, at birth (before and after colostrum intake), every 2 wk from birth to weaning, and every 4 mo from weaning to calving. Green and blue dots indicate BW measurement moments: for dams, weekly during last 2 wk before calving 2; for FO, at birth (before and after colostrum intake), every 2 wk from birth to weaning, and every 2 mo from weaning to calving. The yellow bar for dams indicates the milk yield recording period, including the whole gestation and the last week before dry-off. In addition, the DMI and EB of dams were recorded but are not shown in the figure. Both lactation and growth curve are represented in this figure. The length of the corresponding time intervals and ages is adjusted for visual clarity and does not accurately represent the actual time proportions. The temporal scales should not be interpreted as precise. This figure was created in BioRender.

spring born to those dams (n = 62; 17 from primiparous, 45 from multiparous dams) were followed from birth until 100 DIM after their first calving. Dam-calf pairs were regrouped according to the calving interval (**CInt**) of those dams (**CInt_1**: 324–408 d; **CInt_2**: 409–468 d; **CInt_3**: 469–586 d). The ranges were determined to ensure a similar number of animals per CInt group and a similar number of animals from each parity class within each CInt group.

Management and Sampling

Management. The experiment was conducted at the Dairy Campus research herd (Leeuwarden, the Netherlands) between December 2017 and May 2022. Dams were housed in a freestall. Dams were dried off between 42 and 49 d (40 ± 8.04 d; mean ± SD) before the expected calving date, where expected calving date was based on an expected gestation length of 280 d. At birth, calves were housed at the research farm Dairy Campus (Leeuwarden, the Netherlands). When a calf was born at night the calf was separated in the morning at first milking, approximately from 0500 h. Within the first day after birth, colostrum from the calf's own mother was given twice (2 L each time) by a teat bucket or teat bottle. The first colostrum feeding to the calf occurred 1.67 ± 1.67 h (mean ± SD) after birth. Colostrum quality was assessed using a Brix refractometer (25.3% ± 6.66%; mean ± SD). After colostrum, calves were to milk replacer (Denkamilk Excellent, Denkavit, Voorthuizen, the Netherlands; CP 23% of DM, crude fat 19% of DM) twice daily. The daily volume was gradually increased from 3.5 to 4.5 L by 2 wk of age at a concentration of 125 g/L. Every 2 wk, those calves that were at least 14 d of age and healthy were moved to Dairy Campus young stock farm (Westergeest, the Netherlands) for calf rearing. From 3 wk of age to ~11 wk of age, calves were feed according to a schedule (Supplemental Table S1, see Notes; Wang et al., 2024) based on the young stock rearing protocol. In addition, the calves received ad libitum calf starter feed (Vita Comfort, ForFarmers, Lochem, the Netherlands; CP 16.5% of DM, crude fiber 16% of DM), which is a mixture of

concentrates, chopped short and dedusted wheat straw, and molasses, until ~4 to 4.5 mo of age. After that, the calves were moved to the young cattle barn and offered ad libitum grass silage and finishing pellets. Until 5 to 6 wk before the expected calving date, FO were transported once every 2 wk to Dairy Campus research farm and fed with dry cow ration 4 times per day, with NEL 5.50 MJ/kg of DM. During the first 100 DIM, cows were fed partial mixed ration (**PMR**) with additional concentrate with NEL 6.87 MJ/kg of DM. Concentrate was supplied from the day of calving and increased until 21 DIM to 9 kg/d for primiparous cows and 10 kg/d for multiparous cows, and this level was maintained until 100 DIM. More details about housing and feed management can be found in our previous publications, regarding dams in Burgers et al. (2023) and FO in Wang et al. (2024).

Energy Balance and Dry Matter Intake of Dams. Measurements of DMI and calculations for energy balance (**EB**) were described earlier (Burgers et al., 2023) and available during the last 2 wk before calving 2. In brief, daily intake of PMR was provided 4 times per day and recorded individually by roughage intake control troughs (Hokofarm, Emmeloord, the Netherlands). Concentrate intake was recorded individually using concentrate feeders (Hanskamp, Doetinchem, the Netherlands). Total DMI was calculated by the sum of DMI of PMR and DMI of concentrate. Energy content for the dry cow ration in the last 2 wk before calving was 5.83 ± 0.15 MJ/kg of DM. Weekly EB was calculated according to the intake and requirements of net energy for maintenance and gestation (CVB, 2016). Energy intake, energy requirements, and EB are expressed in kJ/$BW^{0.75}$ per day.

Body Condition and Weight of Dams and Female Offspring. Dams were weighed weekly on the same scale (GEA, Dusseldorf, Germany) during the last 2 wk before expected calving. Female offspring were weighed at birth, once every 2 wk until 12 wk of age around weaning. After that, every 2 mo until ~5 to 6 wk before calving, when FO returned to Dairy Campus research farm. After calving, BW was recorded automatically twice daily after milking as the dam walked over a scale. Body condition score was visually assessed every 4 wk by the same person using a 1 to 5 scale, where 1 is leanest and 5 is fattest (Ferguson et al., 1994). For dams, BCS was assessed once within the last 4 wk before the expected calving date. For FO, BCS was performed every 4 wk after calving.

Blood Sampling of Dams and Female Offspring. Blood from dams was collected weekly from the coccygeal vein into evacuated EDTA tubes (Vacuette, Greiner BioOne, Kremsmunster, Austria) from 2 wk before calving 2 until calving 2, for the analysis of plasma NEFA, BHB, glucose, insulin, and IGF-I concentrations. Blood from FO was collected from the jugular vein in evacuated EDTA and heparin tubes until the calves were about 12 mo old as the jugular vein allows easy access and reliable sampling in young animals, after which the coccygeal vein was used as it is less invasive and more suitable for routine sampling in older animals. Blood samples from FO were taken at birth before (d 0) and after (d 1) colostrum intake, then once every 2 wk for the first 12 wk, then every 4 mo until calving. After collection, blood samples of dams and FO were kept on ice, centrifuged for plasma isolation (3,000 × *g* for 15 min, 4°C), and stored at −20°C.

Milk and Colostrum Sampling of Dams and Female Offspring. Dams during their gestation and FO during the first 100 DIM after their first calving were milked twice daily automatically and milk yield was summed per day. Milk composition of one evening and one morning sample per FO was determined weekly during the first 100 DIM. Milk fat, milk protein, milk lactose percentage, and milk urea concentration were analyzed using MilkoScan FT 6000 spectrometers, and SCC was analyzed using Fossomatic instruments (both from Foss Analytical, Hillerød, Denmark; sample analysis according to method 9622:2013 [ISO, 2013]; Qlip, Zutphen, the Netherlands). The fat- and protein-corrected milk yield (**FPCM**) was calculated as follows (CVB, 2016):

$$\text{FPCM (kg)} = \text{milk yield (kg)} \times [0.337 + 0.116 \times \text{fat (\%)} + 0.06 \times \text{protein (\%)}].$$

This calculation was based on the weekly fat and protein percentages and the mean daily milk yield for each week. Colostrum yield was collected within 2 h after calving 2 (1.06 ± 1.23 h; mean ± SD), as well as the first calving of FO, was recorded (L) and sampled in 10-mL tubes and stored at −20°C.

Analytical Procedures

Blood Variables. Blood analyses were described earlier by Burgers et al. (2023) for dams and by Wang et al. (2024) for FO. In short, plasma insulin and IGF-I concentrations of dams were measured using commercial kits with EDTA blood samples. Insulin was measured using a radioimmunoassay kit (catalog no. PI-12K, EMD Millipore Corporation, Billerica, MA), and IGF-I was measured using an immunoradiometric assay kit (catalog no. A15729, Beckman Coulter, Fullerton, CA). Both assays were quantified by a Gamma Counter (PE Wallac Wizard 1470-020, New York, NY). The blood metabolite concentrations of dams and FO were measured using an autoanalyzer (Cobas Mira, Roche, Switzerland), including growth hormone, glucose, urea, BHB, and NEFA. Natural antibodies (isotypes IgM and IgG) binding to

KLH in plasma of FO were measured using an indirect ELISA with heparin blood samples.

Colostrum Variables: Total Protein, IgG, IgM, Lactoferrin, TGF-β2, and IGF-I. Total protein concentration in colostrum was determined using the Pierce Bicinchoninic Acid Protein Assay Kit (catalog no. 23227, Thermo Scientific, Waltham, MA). The dilution used to measure total protein was 1:400. The total IgM and IgG concentrations in dam and IgG in heifer colostrum were measured with commercial Bovine IgM and IgG ELISA Quantitation Kits (catalog no. E11-101 and E11-118 respectively; Bethyl Laboratories). The dilutions used were determined to be 1:50,000 for IgM and 1:2,000,000 for IgG. The lactoferrin concentration was measured with a Bovine Lactoferrin ELISA Kit (catalog no. E11-126, Bethyl Laboratories). The dilution used for measurement of lactoferrin was determined to be 1:12,000. The concentration of IGF-I in colostrum was determined with a Human IGF-I ELISA kit (catalog no. E20, Mediagnost). The dilution used for IGF-I was determined to be 1:26. The TGF-β2 concentration in colostrum was measured with a Human TGF-β2 ELISA kit (catalog no. DB250, R&D Systems). The dilution used for TGF-β2 was determined to be 1:1,000. The plates were measured with a Multiskan Go reader (Thermo Scientific). The reading wavelength was 562 nm for total protein, 450 nm for IgG, IgM, lactoferrin, TGF-β2, and IGF-I. For IGF-I and TGF-β2, the readings were corrected by subtracting the optical density values measured at wavelength 590 and 570 nm according to the kit protocol, respectively, following the manufacturer's protocol.

Colostrum Variables: Natural Antibodies. Titers of NAb binding keyhole limpet hemocyanin (**KLH**; H8283, Sigma-Aldrich) in colostrum of dams and FO were measured by indirect ELISA according to the method used by de Koning et al. (2015). Briefly, medium-binding plates (Greiner BioOne) were coated with 2 µg/mL KLH in 100 µL of coating buffer (5.3 g/L Na_2CO_3, 4.2 g/L $NaHCO_3$). Plates were incubated overnight at 4°C and subsequently washed with tap water containing 0.05% Tween 20. Serial dilutions for NAb in colostrum samples were done for 8 steps in the antigen-coated plates with PBS (10.26 g/L $Na_2HPO_4 \cdot H_2O$, 2.36 g/L KH_2PO_4, 4.5 g/L NaCl) pH 7.2 containing 0.05% Tween 20 and 1% normal horse serum. One unrelated sample served as a standard control. Natural IgG antibodies in colostrum, binding KLH (KLH-IgG), were detected using 1:10,000 diluted sheep polyclonal anti-bovine IgG-HRP (catalog no. A10–118P, Bethyl Laboratories). Natural IgM antibodies binding KLH (KLH-IgM), were detected with 1:20,000 diluted rabbit polyclonal anti-bovine IgM-HRP (catalog no. A10–100P, Bethyl Laboratories). Natural IgA antibodies binding KLH (KLH-IgA) were detected using 1:10,000 diluted sheep polyclonal anti-bovine IgA-HRP (catalog no. A10–131P, Bethyl Laboratories). The reaction was further developed using a substrate containing tetra methyl benzidine (T0440, Sigma-Aldrich) with 0.05% H_2O_2, and stopped with 50 µL of 1.25 *M* sulfuric acid. Extinctions were measured with a Multiskan Go reader (Thermo Scientific) at a wavelength of 450 nm. Antibody titers were calculated as described by de Koning et al. (2015). Titers were expressed as $\log^2$ values of the dilutions that gave an extinction closest to 50% of E_{max}, where E_{max} represents the highest mean extinction of a standard positive sample present on every microtiter plate (Ploegaert et al., 2007).

Statistical Analysis

Statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC) and R environment (version 4.4.1; R Core Team, 2023). All pairwise relationship analyses are explained in the following sections.

Prepartum Dam Variables Related to Colostrum Variables. Prepartum conditions before dam calving 2, including BW, EB, DMI, blood metabolites during last 2 wk before calving 2, milk yield of the last week before dry-off, total milk yield during the gestation, last BCS (no more than 4 wk) before calving, as well as colostrum variables from dam calving 2, including colostrum yield and colostrum antibodies, growth factors, lactoferrin, and protein were analyzed using a general linear mixed model (PROC MIXED) including the fixed effect of calving interval and parity class of the dam, as well as time and their interactions. The model included a repeated effect of time with dams as repeated subject. A first-order heterogeneous autoregressive covariance matrix (**ARH(1)**) or a first-order autoregressive covariance matrix (**AR(1)**) was selected as the best fit based on the corrected Akaike information criterion and was used to account for within-calf variation. To test relationships between prepartum dam variables and colostrum variables of dam calving 2, means of prepartum dam variables were included, one by one, as covariables in the general linear mixed model (PROC MIXED) to obtain regression coefficient (β) for the colostrum variables (model 1):

$$y_{ij} = \beta dam\_variable + \mu + CInt_i + parity_j + (CInt \times parity)_{ij} + \varepsilon_{ij}, \quad [1]$$

where y_{ij} represents the dependent variables; $\beta dam\_variable$ represents each dam-related variable together with its corresponding regression coefficient; μ represents the mean; $CInt_i$ represents the CInt (i = 1, 2, or 3); $parity_j$ represents the parity class (j = 1 or 2+); $(CInt \times parity)_{ij}$ represents the interaction between CInt and parity class; and ε_{ij} represents the random residual term from a normal

distribution. For BW, EB, DMI, and blood metabolites during the last 2 wk before dam calving 2, the model included a repeated effect of time with dam as repeated subject. An AR(1) was the best fit according to the corrected Akaike information criterion and was used to account for within-dam variation.

Colostrum Variables Related to Female Offspring Variables. Calf plasma variables around colostrum intake, and BW of FO at birth and around weaning were analyzed using a general linear mixed model (PROC MIXED) including the fixed effect of calving interval and parity of the dam. Body weight and blood variables of calves from birth to weaning at 11 wk of age, heifers from weaning to calving at around 25 mo of age, and milk performance of lactating offspring during the first 100 DIM after their first calving were analyzed using a general linear mixed model (PROC MIXED) including the fixed effect of calving interval and parity of the dam, as well as the FO age before calving or the week in milk after calving. To test relationships of colostrum variables between dam calving 2 and FO development from birth to weaning, from weaning to calving, as well as the first 100 DIM after their first calving, means of colostrum variables were included, one by one, as covariables to obtain the regression coefficient (β) for FO variables (model 2 for variables without age repetition, model 3 for variables repeated in age, and model 4 for variables repeated in week in milk):

$$y_{ij} = \beta colostrum\_variable + \mu + CInt_i + parity_j + (CInt \times parity)_{ij} + \varepsilon_{ij}, \quad [2]$$

$$y_{ij} = \beta colostrum\_variable + \mu + CInt_i + parity_j + age_k + (CInt \times parity)_{ij} + (CInt \times age)_{ik} + (parity \times age)_{jk} + \varepsilon_{ij}, \quad [3]$$

$$y_{ijk} = \beta colostrum\_variable + \mu + CInt_i + parity_j + WIM_k + (CInt \times parity)_{ij} + (CInt \times WIM)_{ik} + (parity \times WIM)_{jk} + \varepsilon_{ijk}, \quad [4]$$

where $y_{ij(k)}$ represents the dependent variables; $\beta colostrum\_variable$ represents each colostrum-related variable together with its corresponding regression coefficient; μ represents the mean; $CInt_i$ represents the CInt (i = 1, 2, or 3); $parity_j$ represents the parity class (j = 1 or 2+); age_k represents the age in months of FO (k = 0, 0.5, 1, 1.5, 2, 2.5, 3, 7, 11, 15, 19, 23); $(CInt \times parity)_{ij}$ represents the interaction between CInt and parity class; $(CInt \times age)_{ik}$ represents the interaction between CInt and calf age; $(parity \times age)_{jk}$ represents the interaction between parity class and calf age; $\varepsilon_{ij(k)}$ represents the random residual term from a normal distribution; WIM_k represents the week in milk of lactating offspring (k = 0, 1, 2, 3, 4, 5, 6, 7, 8, 10, 12, 14, 16); $(CInt \times WIM)_{ik}$ represents the interaction between CInt and week in milk; and $(parity \times WIM)_{jk}$ represents the interaction between parity class and week in milk. The model included a repeated effect of time with FO as repeated subject. An ARH(1) or AR(1) was selected as the best fit based on the corrected Akaike information criterion and was used to account for within-calf variation; more details can be found in our previous study (Wang et al., 2024).

Preliminary analysis showed that the model fit based on normality was better using log-transformed data than nontransformed data. Therefore, the regression analyses in both model 2 and model 3 used log-transformed data. To standardize the β for visualization, we first scaled the data using the R scale() function:

$$\beta_i^{'} = \frac{\beta_i}{\sigma(\beta)},$$

where $\beta_i^{'}$ is the scaled regression coefficient for the observation i, β_i represents the original regression coefficient of observation i, and $\sigma(\beta)$ is the standard deviation of the regression coefficients across all observations.

The scaled regression coefficients were further normalized by dividing the maximum absolute value in the scaled dataset to ensure that all values are within the range of [−1, 1]. The normalization was performed using the following formula:

$$\beta_{normalized} = \frac{\beta_i^{'}}{max\left(\left|\beta'\right|\right)},$$

where $\beta_{normalized}$ represents the normalized regression coefficients, $\beta_i^{'}$ represents the scaled regression coefficients, and $max\left(\left|\beta'\right|\right)$ is the maximum absolute value across all β in the matrix. A regression relationship matrix plot was generated using the corrplot() function in R to visualize significant ($P < 0.05$) regression coefficients. The plot was adjusted to display significant relationships only.

Over time significant relationships of variables in both colostrum and offspring plasma were further analyzed. Of all variables, KLH-IgG was the only one that consistently showed a relationship over time. Therefore, FO were categorized into low, medium, and high KLH-IgG groups based on the KLH-IgG titers in the colostrum they received from their dams, with a similar number of animals in each group. The low KLH-IgG group (n = 18) had a mean titer of 8.09 ± 0.46, the medium KLH-IgG group (n = 19) had 9.40 ± 0.32, and the high KLH-IgG

group (n = 19) had 11.27 ± 0.73. Plasma KLH-IgG titers of FO were analyzed over time using a general linear mixed model (PROC MIXED), including the fixed effects of colostrum KLH-IgG group, dam parity, and time (model 5):

$$y_{ijk} = \mu + KLH\text{-}IgG\ Group_i + parity_j + time_k + (KLH\text{-}IgG\ Group \times parity)_{ij} + (KLH\text{-}IgG\ Group \times time)_{ik} + (parity \times time)_{jk} + \varepsilon_{ijk}, \quad [5]$$

where y_{ijk} represents the dependent variables; μ represents the mean; $KLH\text{-}IgG\ Group_i$ represents the colostrum KLH-IgG group (i = low, medium, or high); $parity_j$ represents the parity class of the dam (j = 1 or 2+); $time_k$ represents the age in months of FO (k = 0, 0.5, 1, 1.5, 2, 2.5, 3, 7, 11, 15, 19, 23) or the week in milk of FO after calving (k = 0, 1, 2, 3, 4, 5, 6, 7, 8, 10, 12, 14); $(KLH\text{-}IgG\ Group \times parity)_{ij}$ represents the interaction between the colostrum KLH-IgG group and parity class; $(KLH\text{-}IgG\ Group \times time)_{ik}$ represents the interaction between the colostrum KLH-IgG group and time; $(parity \times time)_{jk}$ represents the interaction between parity class and time; and ε_{ijk} represents the random residual term from a normal distribution. The model included a repeated effect of time with FO as repeated subject. An ARH(1) was selected as the best fit based on the corrected Akaike information criterion and was used to account for within-calf variation.

To test the correlation for colostrum variables between dams (calving 1 and calving 2) and heifers, a Spearman correlation matrix was generated using PROC CORR in SAS, then visualize using the pheatmap function from the pheatmap R package.

Descriptive tables present values as LSM ± maximum SEM or the confidence interval. For the comparison of CInt and its related interactions, P-values of pairwise comparisons of least squares means were corrected with a Tukey adjustment.

RESULTS

There were 62 FO at birth, 59 at weaning, and finally, 53 heifers that started their first lactation. Regarding the number of colostrum samples, there were 39 from dam calving 1, 58 from dam calving 2, and 48 from heifers born to dams with different calving interval (Table 1). The gestation length of the 53 heifers was 277 ± 4.80 d (mean ± SD).

Descriptive Data of Dam Prepartum Variables, Colostrum Variables, and Female Offspring Variables

During the whole gestation, multiparous dams with CInt_1 produced more milk than the other 2 groups (Table 2, 7,302 vs. 5,819 vs. 4,993 ± 320 kg for multiparous dams in CInt_1 vs. CInt_2 vs. CInt_3, $P \leq 0.01$), but not in the primiparous dams (5,880 vs. 5,193 vs. 6,164 ± 495 kg for primiparous dams in CInt_1 vs. CInt_2 vs. CInt_3, $P > 0.10$). Before calving 2, dams with CInt_3 had a greater BCS than dams with CInt_1 ($P < 0.01$). Dams with CInt_2 tended to have a higher BCS than CInt_1 ($P < 0.06$) and lower BCS than CInt_3 ($P < 0.05$). In multiparous dams, CInt_3 tended to have lower BHB than CInt_1 and CInt_2 (0.49 vs. 0.49 vs. 0.40 ± 0.03 mmol/L for dams with CInt_1 vs. CInt_2 vs. CInt_3, respectively; $P = 0.08$ for CInt_3 vs. CInt_1, and $P = 0.06$ for CInt_3 vs. CInt_2), but did not differ in the primiparous dams

Table 1. Number of colostrum samples, dams, and heifer calves per calving interval (CInt) group and parity class of the dam

Item	CInt of dams[1]			Parity class of dams[2]		In total
	CInt_1	CInt_2	CInt_3	Primiparous	Multiparous	
Number of colostrum samples[3]						
Colostrum_C1	13	10	16	8	31	39
Colostrum_C2	18	17	23	16	42	58
Colostrum_FO	17	16	15	15	33	48
Number of dams[4]	19	20	23	17	45	62
Number of heifer calves						
At birth	19	20	23	17	45	62
At weaning	18	19	22	17	42	59
At calving	17	18	18	16	37	53

[1]Calving interval groups include 3 different categories: CInt_1: 324–408 d; CInt_2: 409–468 d; CInt_3: 469–586 d.

[2]Primiparous refers to a dam who has given birth once (parity 1) before extending calving interval; multiparous refers to a dam who has given birth more than once (parity ≥2) before extending calving interval.

[3]Colostrum samples: C1 = dam's calving 1, referring to the calving before VWP treatment; C2 = dam's calving 2, referring to the calving after VWP treatment; FO = female offspring, referring to the female offspring born to dams with different CInt.

[4]Number of dams before calving 2.

Table 2. Prepartum dam variables with different calving intervals (LSM ± maximum SEM or 95% CI)

	Calving interval[1]				*P*-value[2]					
Item	CInt_1	CInt_2	CInt_3	SEM (95% CI)	CInt	Parity	Time	CInt × parity	CInt × time	Parity × time
MY before dry-off[3] (kg/d)	13	10	11	1.04	0.13	0.28	NM	0.27	NM	NM
Total MY of gestation (kg)	6,591^{a}	5,506^{b}	5,579^{b}	288.24	0.01	0.36	NM	<0.01	NM	NM
Last BCS before calving	2.8^{A,b}	3.2^{AB}	3.6^{a,B}	0.15	<0.01	0.03	NM	0.35	NM	NM
2 wk before next calving										
BW (kg)	720	743	743	30.84	0.81	0.68	0.56	0.35	0.67	0.65
NEFA[4] (mmol/L)	0.09	0. 09	0.10	(0.07–0.13)	0.77	0.47	<0.01	0.73	0.76	0.70
BHB (mmol/L)	0.48^{B}	0.55^{A}	0.48^{B}	0.02	0.04	<0.01	0.98	0.04	0.31	0.58
Glucose (mmol/L)	3.59	3.57	3.61	0.05	0.89	0.30	0.88	0.63	0.10	0.42
Insulin (μU/mL)	20.3	21.7	25.2	2.45	0.34	0.87	0.14	0.32	0.67	0.89
IGF-I (ng/mL)	218	222	216	15.8	0.96	<0.01	<0.01	0.57	0.24	0.15
DMI (kg/d)	15.88	15.37	16.13	0.63	0.67	0.95	<0.01	0.60	0.69	0.67
EB (kJ/BW$^{0.75}$)	254.67	239.12	239.23	29.89	0.91	0.61	0.46	0.98	0.78	0.84

^{a,b}Different lowercase superscripts within a row indicate a difference among LSM ($P < 0.05$).

^{A,B}Different uppercase superscripts within a row indicate a trend of a difference among LSM ($0.05 \leq P < 0.1$).

[1]CInt = calving interval; CInt_1: 324–408 d; CInt_2: 409–468 d; CInt_3: 469–586 d.

[2]Time = week before calving for variables assessed during the 2 wk before next calving, specifically including 1 wk and 2 wk before calving. NM = the effect is not in the model.

[3]MY before dry-off = average daily milk yield of the last week before dry-off.

[4]Transformed data are back-transformed, and 95% CI is shown.

(0.48 vs. 0.61 vs. 0.56 ± 0.04 mmol/L for dams with CInt_1 vs. CInt_2 vs. CInt_3, $P > 0.10$). Average daily milk yield in the last week before dry-off and BW, EB, DMI, and plasma NEFA, glucose, and insulin concentrations during the last 2 wk before calving did not differ among CInt groups or parity classes.

Primiparous dams in CInt_2 tended to have lower lactoferrin concentration in colostrum than dams from CInt_3 (Table 3, 1.27 vs. 3.07 ± 0.50 mg/mL, $P = 0.09$), whereas lactoferrin did not differ in multiparous dams with different CInt (2.79 vs. 2.43 vs. 1.79 ± 0.37 mg/mL for dams with CInt_1 vs. CInt_2 vs. CInt_3, $P > 0.10$). Primiparous dams had lower Brix values (25.28% vs. 27.44% ± 0.72%, $P = 0.01$), lower concentrations of total IgM (5.31 vs. 8.27 ± 1.11 mg/mL, $P = 0.02$), lower total IgG (99.83 vs. 189.31 ± 20.91 mg/mL, $P < 0.01$), lower total protein (240.65 vs. 290.82 ± 13.70 mg/mL, $P < 0.01$), lower TGF-β2 (LSM 250.56 vs. 413.72, CI 191.41–489.21 ng/mL, $P < 0.01$), and lower titers of KLH-IgG (8.85 vs. 10.00 ± 0.36, $P < 0.01$) and KLH-IgA (9.19 vs. 9.97 ± 0.29, $P < 0.01$) in colostrum, than multiparous dams. Overall, CInt had no effect on any of the colostrum variables of dams.

Female offspring variables before and after colostrum intake, from birth to calving, and after calving are presented in Supplemental Table S2 and S3 (see Notes). Be-

Table 3. Colostrum variables (C2) of dams with different calving intervals (LSM ± maximum SEM or 95% CI)

	Calving interval[1]				*P*-value		
Item[2]	CInt_1	CInt_2	CInt_3	SEM (95% CI)	CInt	Parity	CInt × parity
Yield (L)	5.0	5.8	4.7	0.74	0.52	0.43	0.18
Brix value (%)	26.1	27.0	25.9	0.77	0.52	0.01	0.42
Lactoferrin (mg/mL)	2.38	1.85	2.43	0.32	0.29	0.50	<0.01
IGF-I (ng/mL)	994	906	906	30.68	0.89	0.43	0.78
TGF-β2[3] (ng/mL)	340.73	324.70	336.20	(253.89–452.19)	0.60	<0.01	0.51
Total protein (mg/mL)	264.81	265.14	267.26	15.33	0.99	<0.01	0.78
Total IgG (mg/mL)	134.8	152.4	146.6	23.10	0.85	<0.01	0.78
Total IgM (mg/mL)	7.9	5.8	6.7	1.22	0.44	0.03	0.95
NAb							
KLH-IgM	12.98	12.88	12.78	0.16	0.64	0.35	0.99
KLH-IgG	9.81	9.20	9.27	0.39	0.46	<0.01	0.83
KLH-IgA[3]	9.81	9.33	9.40	(8.85–10.42)	0.44	0.03	0.11

[1]CInt = calving interval; CInt_1: 324–408 d; CInt_2: 409–468 d; CInt_3: 469–586 d.

[2]NAb = natural antibodies; KLH = keyhole limpet hemocyanin. Unit for all antibodies against KLH is titer.

[3]Transformed data are back-transformed, and 95% CI is shown.

fore colostrum intake, calves born to primiparous dams had lower titers of KLH-IgM ($P < 0.01$) and KLH-IgG ($P = 0.03$) in plasma than those born to multiparous dams. After colostrum intake, plasma KLH-IgG titers were higher in calves born to CInt_1 than CInt_3 ($P = 0.05$). The remaining offspring variables from birth to weaning, from weaning to calving, and during the first 100 DIM in Supplemental Table S2 and S3 were previously reported (Wang et al., 2024).

Prepartum Dam Variables Related to Colostrum Variables

A higher BCS of dams before calving was related to lower lactoferrin concentration in colostrum (β = −0.70, Figure 2). Higher DMI of dams during last 2 wk before calving was related to greater IGF-I (β = 0.26) and total protein (β = 0.33) concentrations in colostrum. A more positive EB prepartum was related to lower colostrum yield (β = −0.21), and higher titers of total IgM concentration (β = 0.43) and KLH-IgM titers (β = 0.14) in colostrum. Higher milk yield during the whole gestation was related to higher lactoferrin concentration in colostrum (β = 0.63). Higher daily milk yield during the last week before dry-off was related to higher IGF-I (β = 0.17) and TGF-β2 (β = 0.33) concentrations in colostrum. Higher plasma NEFA concentration before calving was related to higher colostrum yield (β = 0.17). Body weight, plasma IGF-I, insulin, glucose, and BHB concentrations in dams before calving were not related to colostrum variables.

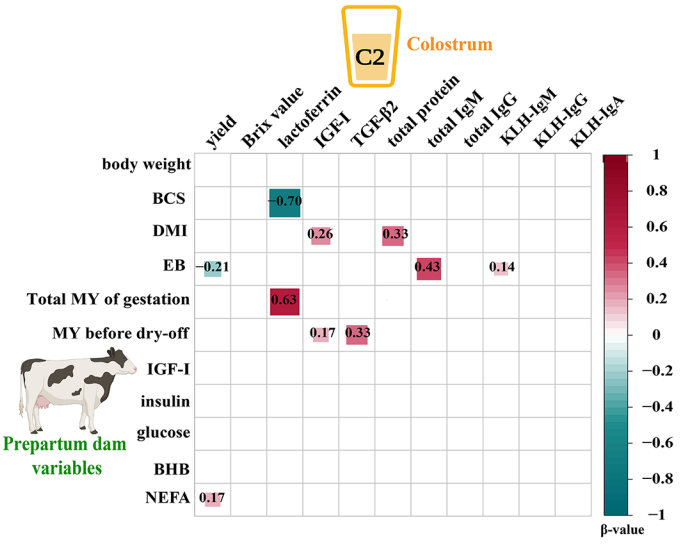

Figure 2. Regression coefficients between prepartum dam variables and colostrum variables. The MY before dry-off indicates the average daily milk yield during the last week before dry-off. C2 = colostrum from dam calving 2; calving 2 means the calving after VWP treatment. The colored cells represent these regression coefficients, with the color intensity reflecting the strength and direction of the relationship. The color bar on the right indicates the range of the regression coefficients. The numbers displayed within some cells represent the magnitude of these coefficients and are shown only for significant *P*-values ($P < 0.05$). The cow image was created in BioRender.

Colostrum Variables Related to Female Offspring from Birth to Lactation

Calf: From Birth to Weaning. For calf BW, greater total protein concentration in colostrum was related to heavier calves at birth (β = 0.59, Figure 3). Colostrum variables were not related to mean BW, weaning weight, and BW gain of calves from birth to weaning.

For calf plasma hormones and metabolites, higher KLH-IgM (β = 0.97) titers in colostrum was related to higher plasma growth hormone concentration in calves. Higher total IgM concentration in colostrum was related to lower glucose (β = −0.14) and higher urea (β = 0.19) concentration in calf plasma from birth to weaning. Lower colostrum yield (β = −0.07), and higher concentration of IGF-I (β = 0.08) and TGF-β2 (β = 0.09) in dam colostrum were related to higher plasma NEFA concentration in calves from birth to weaning. Colostrum variables were not related to plasma insulin and IGF-I concentration in calves from birth to weaning.

For calf plasma NAb, higher colostrum yield (β = 0.06), higher total IgM concentration (β = 0.12), and higher KLH-IgG titers (β = 0.36) in dam colostrum were related to higher KLH-IgM titers in calf plasma from birth to weaning. Higher Brix value (β = 0.24), higher total IgM concentration (β = 0.09), and higher NAb-KLH titers (β = 0.62, 0.50, 0.55) in colostrum were related to higher KLH-IgG titers in calf plasma from birth to weaning. Before colostrum intake, there were no relationships between colostrum variables and NAb-KLH in calf plasma. After colostrum intake, total IgM concentration and KLH-IgG titers in dam colostrum were positively related to KLH-IgG and IgM titers in calf plasma. Regarding the differences of KLH-IgG and IgM titers in calf plasma before and after colostrum intake, all tested antibodies in dam colostrum, excluding total IgG concentration and KLH-IgM titers, were positively related to the differences of KLH-IgG and IgM titers in calf plasma.

Heifer: From Weaning to Calving. For heifer BW, greater total protein concentration (β = 0.53) and higher KLH-IgG titers (β = 0.51) in dam colostrum were related to heavier heifers from weaning to calving.

For heifer plasma hormones and metabolites, greater total IgG concentration (β = −0.12) and KLH-IgA (β = −0.46) titers in dam colostrum were related to lower insulin concentration in heifer plasma. Higher Brix value in colostrum was related to lower growth hormone (β = −0.61) and higher IGF-I (β = 0.65) concentration in heifer plasma from weaning to calving. The opposite relationships were found between lactoferrin concentration

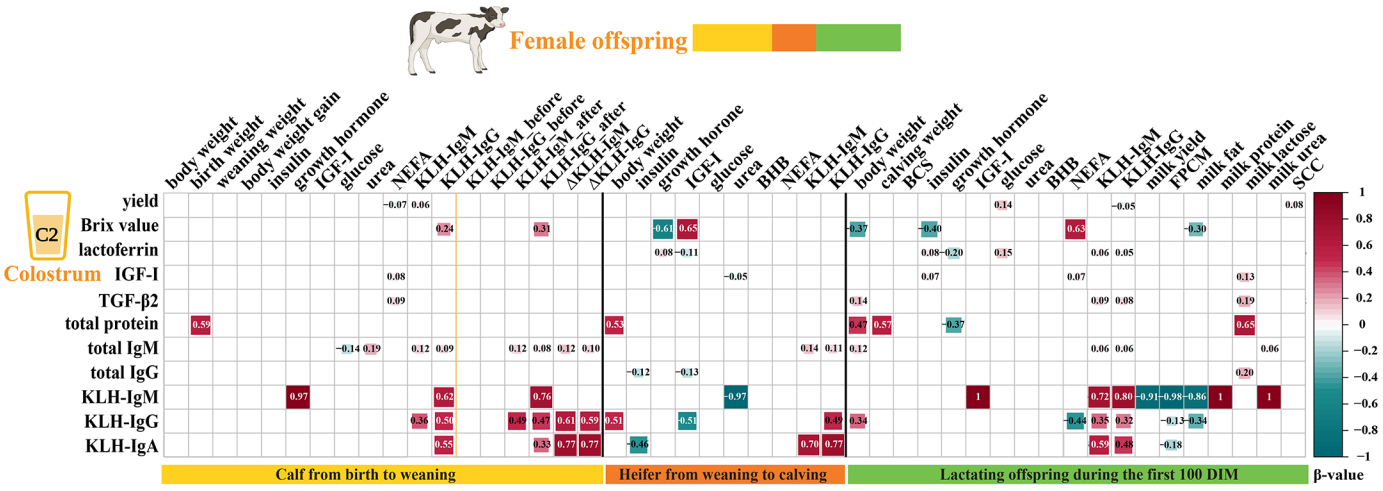

Figure 3. Regression coefficients between dam colostrum variables and female offspring variables from birth to weaning, from weaning to calving, and during the first 100 DIM. C2 = colostrum from dam calving 2; calving 2 means the calving after VWP treatment. Δ = the difference between before and after colostrum intake. The colored cells represent these regression coefficients (β), with the color intensity reflecting the strength and direction of the relationship. The color bar on the right indicates the range of the regression coefficients. The numbers displayed within some cells represent the magnitude of these coefficients and are shown only for significant *P*-values ($P < 0.05$). This figure was created in BioRender.

in colostrum and growth hormone (β = 0.08) and IGF-I (β = −0.11) concentration in heifer plasma. Higher total IgG (β = −0.13) and KLH-IgG (β = −0.51) were related to lower IGF-I concentration in heifer plasma. Higher IGF-I concentration (β = −0.05) and higher KLH-IgM titers (β = −0.97) in colostrum were related to lower urea concentration in heifer plasma. Colostrum variables were not related to glucose, BHB, or NEFA concentration in heifer plasma from weaning to calving.

For heifer plasma NAb, greater total IgM concentration (β = 0.14, β = 0.11) and higher titers of KLH-IgA (β = 0.70, β = 0.77) in colostrum were related to lower KLH-IgM and KLH-IgG titers in heifer plasma. Higher KLH-IgG titers in dam colostrum were related to higher KLH-IgG titers in heifer plasma.

Lactating Offspring: First 100 DIM. For lactating offspring body condition, lower Brix value (β = −0.37), higher TGF-β2 (β = 0.14), higher total protein (β = 0.47), higher total IgM concentration (β = 0.12), and higher KLH-IgG titers (β = 0.34) in dam colostrum were related to higher mean BW during the first 100 DIM. Higher total protein concentration (β = 0.57) in dam colostrum was related to heavier lactating offspring at calving. Colostrum variables were not related to BCS of lactating offspring.

For plasma hormones and metabolites in lactating offspring, lower Brix value (β = −0.40), higher lactoferrin (β = 0.08), and higher IGF-I (β = 0.07) concentration in dam colostrum were related to higher plasma insulin concentration in lactating offspring. Lower lactoferrin (β = −0.20) and total protein (β = −0.37) in dam colostrum were related to higher growth hormone concentrations in lactating offspring. Higher KLH-IgG titers (β = 1) in dam colostrum was related to higher plasma IGF-I concentration in lactating offspring. Higher colostrum yield (β = 0.14) and greater lactoferrin concentration (β = 0.15) in dam colostrum were related to higher plasma glucose concentration in lactating offspring. Higher Brix value (β = 0.63) and IGF-I concentration (β = 0.07), and lower KLH-IgG titers (β = −0.44) in dam colostrum were related to higher plasma NEFA concentration in lactating offspring. Colostrum variables were not related to plasma urea and BHB concentration in lactating offspring.

For plasma NAb in lactating offspring, higher lactoferrin (β = 0.06, 0.05 with KLH-IgM and KLH-IgG, respectively), TGF-β2 (β = 0.09, 0.08), total IgM concentrations (β = 0.06, 0.06), NAb-KLH titers (β = 0.72, 0.80, β = 0.35, 0.32, β = 0.59, 0.48) in colostrum were related to higher titers of KLH-IgM and IgG in lactating offspring plasma. Moreover, higher colostrum yield (β = −0.05) was related to lower KLH-IgG titers in lactating offspring plasma.

For milk production in lactating offspring, lower KLH-IgM titers in dam colostrum was related to higher milk yield (β = −0.91) and FPCM (β = −0.98) in lactating offspring. Furthermore, lower KLH-IgG (β = −0.13) and KLH-IgA (β = −0.18) titers were related to higher FPCM in lactating offspring. Lower Brix value (β = −0.30), and lower KLH-IgM (β = −0.86) and KLH-IgG (β = −0.34) titers in dam colostrum were related to higher milk fat content in lactating offspring. Higher KLH-IgM titers in dam colostrum were related to higher milk protein content (β = 1) and milk urea concentration (β = 1) in lactating offspring. Greater IGF-I (β = 0.13), TGF-β2 (β

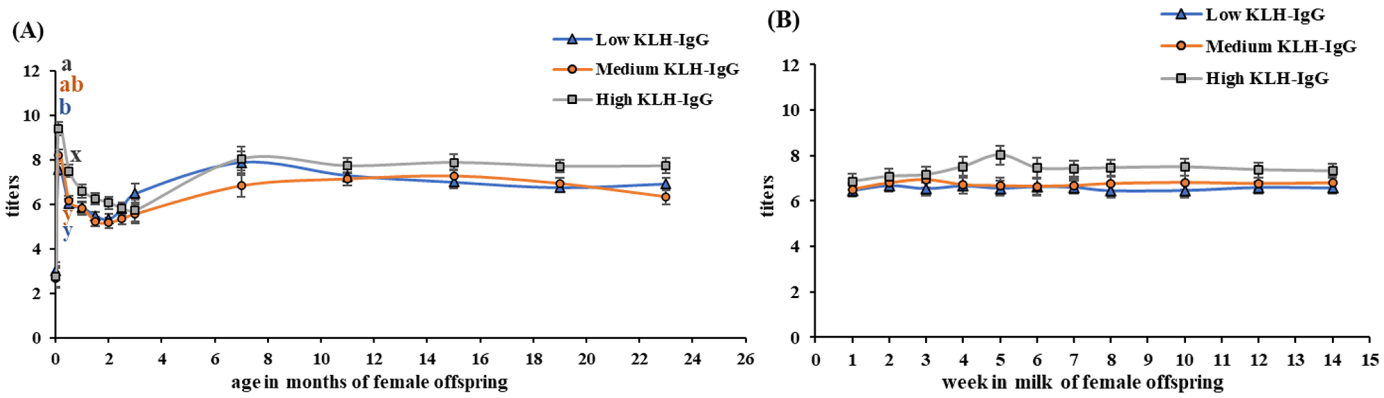

Figure 4. Variable KLH-IgG titers in both colostrum and female offspring plasma over time (A) from birth to calving and (B) during the first 100 DIM of lactation. Low KLH-IgG group indicates the female offspring fed colostrum with low levels of KLH-IgG. Medium KLH-IgG group indicates the female offspring fed colostrum with medium levels of KLH-IgG. High KLH-IgG group indicates the female offspring fed colostrum with high levels of KLH-IgG. Data were derived from a Mixed model including colostrum KLH-IgG group, dam parity, time, and their 2-way interactions. Different letters (a, b or x, y) indicate a difference among LSM of groups ($P < 0.05$) at one sampling moment: a, b after colostrum intake; x, y at 1 wk of age.

= 0.19), total protein (β = 0.65), and IgG (β = 0.20) concentration in dam colostrum were related to higher milk lactose content in lactating offspring. Colostrum yield (β = 0.08) was positively related to milk SCC in lactating offspring.

Colostrum Variables Related to Female Offspring Over Time from Birth to Lactation. Just after colostrum intake, calves fed with high titers of KLH-IgG colostrum had significantly higher KLH-IgG titers in their plasma, compared with calves fed with low KLH-IgG colostrum. In addition, at 1 wk of age, calves in the high KLH-IgG group had significantly higher titers KLH-IgG in their plasma, compared with those in the low and medium KLH-IgG groups. Thereafter, plasma KLH-IgG titers of FO in the high KLH-IgG group was always numerically higher than the other 2 groups, even during lactation (Figure 4).

Colostrum Variable Repeatability Over Lactation and Across Generations. Most colostrum variables, at dam calving 1 (**C1**) were related to colostrum variables at dam calving 2 (**C2**), excluding colostrum yield, lactoferrin, IGF-I, and total IgG concentrations (Figure 5). Colostrum yield of the dam (C1) was strongly correlated with the colostrum yield of their FO. No further relationships in colostrum were present between dams and their offspring.

Heifers born to dams with CInt_3 had lower total IgG concentration in colostrum after their first calving than CInt_1, and tended to have lower total IgG concentration than CInt_2 (Table 4). Colostrum KLH-IgG titers (9.58 vs. 8.61 ± 0.43) tended to be higher in heifers born to primiparous dams than multiparous dams. Colostrum yield, Brix value, total protein concentration, KLH-IgM, and KLH-IgA titers of colostrum of the young heifers were not influenced by calving interval, or parity class of the dam.

DISCUSSION

The objective of the study was to investigate the relationship between dams, colostrum, and FO. In the current study, dams with high EB during the precalving period produced lower colostrum yield but with high antibody IgM levels, and that in turn was related to offspring with high plasma NAb-KLH levels from birth until lactation.

Prepartum Dam Variables Related to Colostrum Variables

Prepartum dam variables including energy status and milk yield in the last 2 wk before calving had some relationships with colostrum variables, including nutrients and biologically active substances. Higher prepartum BCS in dams was related to lower lactoferrin concentration in colostrum. However, prepartum BCS did not affect total IgG, IgM concentrations, or NAb level in colostrum, in contrast to a previous study reporting that prepartum BCS was positively related to IgG concentration in colostrum (Immler et al., 2022). The contrast was probably caused by the difference in defining the BCS in both studies; Immler et al. (2022) used cows with a variable health status, with one-twelfth of the cows classified with a low BCS (<3), whereas our study included one-fourth of the dams with BCS <3. In addition, NAb entails a proportion of the total IgG content in colostrum, and NAb followed a trend similar to that of total IgG, as also reported by Mayasari et al. (2015). Natural antibodies, produced by B cells, likely act as a first-line immune

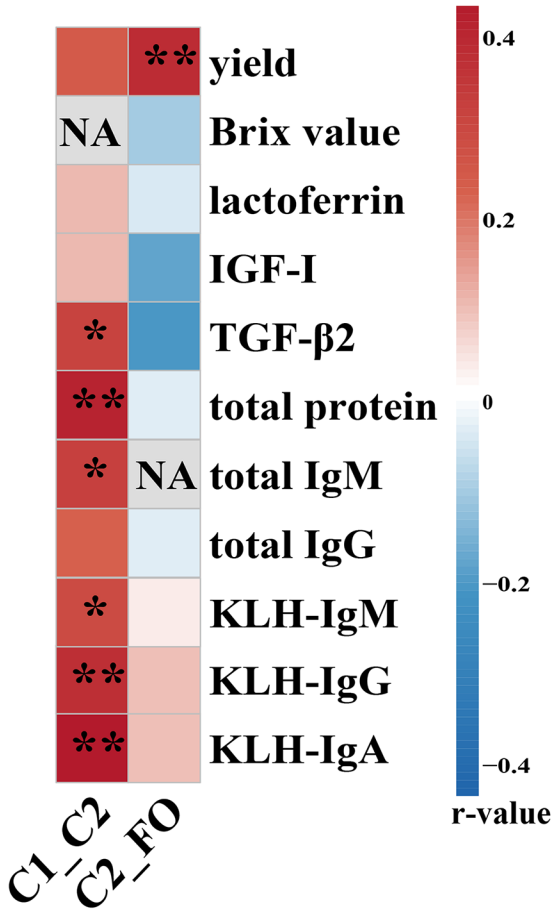

Figure 5. Spearman correlation coefficients in colostrum variables between dams in calving 1 (C1), calving 2 (C2), and their female offspring (FO). The colored cells represent these correlation coefficients (r), with the color and its intensity reflecting the direction and strength of the relationship. The color bar on the right indicates the range of the correlation coefficients. Significance is denoted by asterisks: *$P < 0.05$, and **$P < 0.01$. Nonsignificant correlations are left blank. KLH = keyhole limpet hemocyanin; TGF-β2 = transforming growth factor-β2; NA = data were not available.

defense against infections. The effector functions of B cells are preferentially fueled by oxidative metabolism, glycolysis, and amino acid utilization (Ganeshan and Chawla, 2014). Therefore, another possible explanation for the lack of relationship between maternal BCS and antibodies in colostrum is that the synthesis of antibodies primarily depends on the function of the immune system, rather than on the dam's metabolic status when all dams are healthy and have adequate nutrition. Moreover, the lack of relationship between dams and colostrum in our study could be attributed to the variation of interval between calving and colostrum collection (1.06 ± 1.23 h; mean ± SD); as the colostrum volume increases within the first few hours after calving, its quality tends to decrease due to dilution (Moore et al., 2005; Morin et al., 2010).

Higher DMI in dams before calving was related to greater IGF-I and total protein concentrations in colostrum. Higher EB in dams before calving was related to lower colostrum yield and higher total IgM and KLH-IgM titers in colostrum. Dams with higher prepartum DMI or a more positive EB may have partitioned more energy toward body reserves, such as fat and muscle, rather than colostrum synthesis. This partitioning could limit nutrient availability for mammary gland activity and colostrum production during the critical transition period (Davis and Collier, 1985; Gross, 2022), as colostrogenesis starts 3 to 4 wk before parturition (Baumrucker and Bruckmaier, 2014). Subsequently, the lower colostrum yield could result in a more concentrated composition (Silva-Del-Río et al., 2017), which partially explained the positive relationship between prepartum DMI, EB, and colostrum composition. In addition, plasma NEFA, which is considered to be an indicator for body fat mobilization and negative EB, was positively related to colostrum yield in the current study, but not related to colostrum components, including Ig and NAb. However, van Knegsel et al. (2007) reported a positive relationship between peripartum plasma NEFA concentration from wk −3 to 9 relative to calving and milk NAb. The contrast between these 2 studies could be attributed by sampling moments and sample type, whether colostrum or milk. As explained previously, Burgers et al. (2023) reported a greater NEFA concentration after calving than before calving, and the changing trend over time of NEFA was opposite before and after calving. Notably, the immunological properties of colostrum differ significantly from that of milk (Puppel et al., 2019). In addition, in our study, we used the CVB (2016) system to calculate EB to align with local practices, and caution is needed when the current results are compared with other net energy evaluation systems, such as the NASEM (2021) system.

Greater milk yield of dams before calving was related to higher concentrations of lactoferrin, IGF-I, or TGF-β2 in colostrum. Greater total milk yield during the whole gestation and daily milk yield of the last week before dry-off could reflect the well-developed mammary gland with fully differentiated secretory cells (Strucken et al., 2015), which could promote the secretion of bioactive components in colostrum, such as lactoferrin, IGF-I, and TGF-β2 (Baumrucker and Blum, 1993; Schanbacher et al., 1993).

Colostrum Variables Related to Female Offspring Variables

Before colostrum intake, no relationships were found between NAb in colostrum and NAb in calf plasma. After colostrum intake, the NAb titers in plasma of calves increased directly, indicating that they are likely derived

Table 4. Colostrum variables (FO) of lactating offspring born to dairy dams with different calving interval (LSM ± maximum SEM or 95% CI)

	Calving interval[1]				*P*-value		
Item[2]	CInt_1	CInt_2	CInt_3	SEM (95% CI)	CInt	Parity	CInt × parity
Yield (L)	3.9	4.1	3.9	0.65	0.96	0.21	0.67
Brix value (%)	26	23	23	1.95	0.34	0.23	0.72
Lactoferrin[3] (mg/mL)	0.31	0.34	0.26	(0.21–0.42)	0.31	0.91	0.82
IGF-I (ng/mL)	557	626	582	56.23	0.61	0.21	0.22
TGF-β2[3] (ng/mL)	180.22	178.00	179.58	(138.89–232.20)	0.99	0.38	0.83
Total protein (mg/mL)	269.93	269.99	238.58	17.07	0.31	0.44	0.74
Total IgG (mg/mL)	65.7[a]	57.3[A]	38.6[b,B]	6.57	0.01	0.89	0.36
NAb							
KLH-IgM	13.40	13.40	13.23	0.20	0.77	0.12	0.89
KLH-IgG	9.20	8.98	9.20	0.54	0.92	0.06	0.80
KLH-IgA	9.65	9.32	9.15	0.22	0.19	0.33	0.39

[a,b]Different lowercase superscripts within a row indicate a difference among LSM ($P < 0.05$).

[A,B]Different uppercase superscripts within a row indicate a trend of difference among LSM ($0.05 \leq P < 0.1$).

[1]CInt = calving interval; CInt_1: 324–408 d; CInt_2: 409–468 d; CInt_3: 469–586 d.

[2]NAb = natural antibodies; KLH = keyhole limpet hemocyanin. Unit for all antibodies against KLH is titer.

[3]Transformed data are back-transformed, and 95% CI is shown.

from colostrum (Srinivasan et al., 1999; Mayasari et al., 2016). In addition, positive relationships were found between NAb in dam colostrum and calf plasma after colostrum intake until their first calving moment. In line with our current study, levels of neonatal NAb during the early weeks of life were related to levels of maternal NAb obtained via colostrum (Mayasari et al., 2016; Mayasari, 2017). The positive relationship between total IgM concentration rather than IgG in dam colostrum and NAb titers of IgM and IgG in calf plasma from birth to weaning may reflect the role of IgM in the primary immune response (Ouchida et al., 2012). Natural IgM is, in particular, part of the first line of defense, due to formation of immune complexes with pathogenic microorganisms (Boes, 2000). These immune complexes subsequently activate the classical complement pathway leading to enhanced phagocytosis and antigen presentation, which will finally stimulate production of specific antibodies. However, in the current study there was no relationship between colostrum IgG and calf plasma NAb titers. It is likely that endogenous IgG is poorly produced before weaning due to negative feedback by maternal IgG (Van de Perre, 2003). Furthermore, for class switch from IgM to IgG specific cytokines are needed, which are probably not produced in sufficient quantities by the not fully developed calf immune system. In addition, the volume of colostrum provided at the first feeding in our study was below the standard recommendation of 4 L (NASEM, 2021), which could limit its effects. Future studies are needed to understand the role of colostrum IgG and IgM on calf immune development, and to explore their impact during weaning and rearing periods.

Because all calves were provided the same amount of colostrum (2 × 2 L), the relationship between colostrum yield and calf plasma NEFA and KLH-IgM could be attributed to first the maternal condition during fetal development (Wang et al., 2025). As BW at birth was measured immediately at birth before colostrum intake, greater total protein concentration in colostrum related to greater calf birth weight could result from the maternal conditions during gestation (Zhang et al., 2002). In addition, higher colostrum yield may dilute its components (Pritchett et al., 1991; Röder et al., 2023), reducing nutrient content, which may affect calves. Higher Brix value of dam colostrum was related to higher plasma NAb-IgG in calves after colostrum intake and for the total period from birth to weaning, but the Brix value was not related to calf NAb-IgM. A higher Brix value in dam colostrum reflects a higher content of the dominant immunoglobulin, IgG, which enhances the passive transfer of IgG to the calf, leading to higher NAb-IgG titers in the calf plasma. However, because IgM is primarily produced by the calf's own immune system (Butler, 1969), the IgM concentration in plasma is probably less influenced by colostrum. Higher concentrations of IGF-I and TGF-β2 in colostrum were related to higher plasma NEFA concentration in calves from birth to weaning. Colostrum, enriched with growth factors, can stimulate the growth of lean muscle tissue and prompt the body to use energy (Ramani et al., 2024), potentially increasing plasma NEFA concentration. In the heifer's later life, higher protein concentration in colostrum was related to greater BW from weaning to calving, but not before calving. Supported by the previous studies, the effect of colostrum on calf BW appears strongest in calves during the 70 to 105 d of age and can extend up to 180 d (Robison et al., 1988). Colostrum intake in early feeding affected postweaning BW gain (Soberon and van Amburgh, 2011).

During later growth stages, the differences in muscle and skeletal development, which take time to manifest, begin to emerge more distinctly.

After calving, FO, fed colostrum with lower NAb-KLH titers at birth, had lower NAb-KLH titers in plasma but yielded more milk and FPCM with a greater milk fat content than those fed colostrum with higher NAb-KLH titers. This indicates a developmental trade-off, where reduced passive immunity at birth allows more energy for mammary development, which normally processes from the 3 mo of fetus to calves 6 mo of age (Wallace, 1953). Given that NAb was measured repeatably in bovine plasma within cows over time (Ploegaert et al., 2011), NAb levels had a high genetic basis with the heritability for NAb-KLH of 0.42 within herds (Ploegaert et al., 2010). In addition, milk yield of an individual cow is affected by both her genetic background (20%–30%), as well as her environment (70%–80%; van Amburgh and Soberon, 2013). This observed relationship between NAb in colostrum and offspring plasma and milk production may reflect underlying genetic or developmental programming differences established early in life (de Klerk et al., 2015). Calves with lower IgG concentration in serum were more susceptible to infections, which caused a long-term effect on lactation (DeNise et al., 1989). Each unit of serum IgG increase resulted in an 8.48-kg increase in milk production. However, in the current study we observed a negative association between colostral antibody levels and offspring milk yield. Total IgM concentration in colostrum was related to KLH-IgM and IgG from birth to lactation. Higher NAb titers in offspring developed in early life had a long-term imprinting of their B cell repertoire by maternal antibodies, particularly the mature follicular compartment (Fink et al., 2008). The KLH-IgG titers in dam colostrum and offspring plasma were positively related to each other from birth to lactation, but KLH-IgM titers in dam colostrum and offspring plasma were not related to each other before the offspring's calving. The difference in long-term persistence between NAb-IgM and NAb-IgG could be due to the circulating levels of 2 NAb isotypes varying in individuals and the presence of the idiotypic network (Lundkvist et al., 1989).

Colostrum Variable Repeatability Over Lactation and Across Generations

Colostrum composition at the first calving in the experiment was highly related to colostrum composition at the second calving in the experiment. Positive relationships between colostrum composition between 2 calvings align with previous studies where they reported the link between colostrum composition across parities and the genetic background (Haile-Mariam et al., 2003; Ploegaert et al., 2010; Gross et al., 2016), endocrine regulation, and homeostasis (Westhoff et al., 2024). Colostrum yield, and a few colostrum components in dams and their offspring, were related to each other. Another study reported significant genetic correlations within colostrum components, including protein content, lactose content, and total solids, but not with yield (Soufleri et al., 2019). One possible reason for the contrasting relationship between colostrum composition and yield could be the difference in study size: 49 individual dam-offspring pairs in our study and herd-level with 1,074 cows in the earlier study (Soufleri et al., 2019). Additionally, the substantial variation in genetic potential for colostrum composition in offspring reflected the complexity of gene–environment interactions, with environmental factors such as sire effects and differences in farming practices playing a role (Soufleri et al., 2025). Therefore, improving offspring colostrum quality requires a combination of genetic and environmental interventions, such as enhanced sire selection, nutrition, and health monitoring to holistically boost colostrum quality and immune function.

Limitations and Implications

The value in the current study lies in the long-term monitoring of dams, including their colostrum characteristics and their offspring over lactations and generations. A limitation of this study is the relatively small number of animals. The small number of animals is partly due to the retrospective nature of this study where we specifically monitored the FO of the original study including 154 dams. In addition, we monitored the offspring from the dam for at least 1 yr, and subsequently we tracked them for another 2 yr, resulting in a limited number of FO available after a minimum of 3 yr. In addition, relationships between dam, colostrum, and FO in the study could be partially attributed to both genetic and physiological mechanisms. Our current study does not clearly differentiate between genetics and epigenetics; recognizing their potential interplay is essential. Further research should aim to investigate genetic and physiological influences in the long-term maternal effects. Additionally, a strictly controlled experiment with a large number of animals is required to evaluate the relationships in colostrum variables across lactations and across generations. Overall, the findings of this study indicate that prepartum management is important for subsequent colostrum composition, which will further affect the offspring in early life but not the colostrum of offspring.

CONCLUSIONS

In the current study, higher EB in prepartum dam during the 2 wk before calving was related to better colostrum

quality. Dams with higher DMI before calving produced colostrum with higher IGF-I and protein concentrations. In addition, higher milk production before dry-off was related to higher growth factor concentrations in colostrum, which in turn corresponded to higher NEFA and lower glucose concentrations in calf plasma from birth to weaning. Higher NAb levels in dam colostrum were related to greater NAb levels in FO from birth through weaning till calving. Colostrum composition across different parities for the same dam were highly comparable, while the relationships of colostrum variables between dams and their FO were limited.

NOTES

The authors thank the China Scholarship Council (Beijing, China) for the scholarship received by Yapin Wang. This study was financed by Dutch dairy cattle fund (Melkveefonds, Wageningen, the Netherlands) and Samenwerkingsverband Noord-Nederland (SNN), Ruimtelijk Economisch Programma (Groningen, the Netherlands). The authors thank the staff of the Dairy Campus research farm (Leeuwarden, the Netherlands) for their work and dedication during the experiment. Supplemental material for this article is available at https://doi.org/10.5281/zenodo.17356491. The experimental protocol was approved by the Institutional Animal Care and Use Committee of Wageningen University & Research (Wageningen, the Netherlands) and complied with the Dutch law on animal experimentation (approval number: AVD401002016653). The authors have not stated any conflicts of interest.

Nonstandard abbreviations used: AR(1) = first-order autoregressive covariance matrix; ARH(1) = first-order heterogeneous autoregressive covariance matrix; C1 = colostrum from dam calving 1; C2 = colostrum from dam calving 2; CInt = calving interval; CInt_1: 324–408 d; CInt_2: 409–468 d; CInt_3: 469–586 d; EB = energy balance; FO = female offspring; FPCM = fat- and protein-corrected milk yield; HRP = horseradish peroxidase; KLH = keyhole limpet hemocyanin; MY = milk yield; NAb = natural antibodies; NEFA = nonesterified fatty acids; PMR = partial mixed ration; TGF = transforming growth factor; VWP = voluntary waiting period.

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