#### RESEARCH ARTICLE

# The effect of failed transfer of passive immunity and agammaglobulinemia on the occurrence of preweaning diarrhea, pneumonia, and mortality in Holstein calves

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#### Abstract

Aim of study: To evaluate the effect of failed transfer of passive immunity (FPI; Brix% < 8, equivalent to serum immunoglobulin G < 10.1 g/L) and agammaglobulinemia (AG; Brix%  $\leq 6.5$ , equal to 0 g/L serum immunoglobulin G) assessed with a digital Brix refractometer on the occurrence of pre-weaning diarrhea, pneumonia and mortality in Holstein female calves.

Area of Study: Hot-arid zone of northern Mexico (25 °N).

*Material and methods*: Health events and mortality records were obtained from Holstein calves (n = 4,349) in a large commercial dairy herd. Multiple logistic regression analyses were used to model the effect of the failure of passive transfer of maternal immunoglobulins or AG on preweaning diarrhea, pneumonia, and mortality of Holstein calves.

*Main results*: Calves with FPI 24 h post-calving had 1.9 greater odds of presenting preweaning diarrhea than herd-mates not having FPI. Agammaglobulinemic calves were 2.6 times more likely to suffer preweaning diarrhea than calves not having this condition. Calves with FPI had 1.4 greater odds of having preweaning pneumonia than calves not presenting FPI. Calves with AG were 2.1 times more likely to get pneumonia than those with no AG. Episodes of diarrhea predisposed calves to pneumonia (odds ratio= 3.8). The odds of dying before 60 days of age were 1.9 times higher in calves with FPI.

Research highlights: These results reaffirm that FPI and AG 24 h post-calving increase the risk of preweaning diarrhea and pneumonia; also, diarrhea is a significant risk factor for pneumonia. These diseases alone or co-occurring in the calves markedly increase preweaning mortality.

keywords: epidemiology; passive transfer; refractometer; immunoglobulin; dairy calf.

# Efecto de la transferencia fallida de inmunidad pasiva y la agammaglobulinemia sobre la ocurrencia de diarrea, neumonía y mortalidad antes del destete en becerras Holstein

#### Resumen

Objetivo del estudio: Evaluar el efecto de la transferencia fallida de inmunidad pasiva (TFIP; Brix% <8, equivalente a inmunoglobulina sérica G sérica <10.1 g/L) y agammaglobulinemia (AG; Brix% ≤ 6.5, igual a 0 g/L de inmunoglobulina sérica G) evaluado con un refractómetro Brix digital sobre la ocurrencia pre-destete de diarrea, neumonía y mortalidad en becerras Holstein.

Área de Estudio: Zona caliente y árida del norte de México (25 °N).

Materiales y métodos: Se obtuvieron registros de eventos de salud y mortalidad de becerras Holstein (n = 4,349) en un hato lechero comercial extenso. Se llevaron a cabo análisis de regresión logística múltiple para modelar el efecto de la falla de la transferencia pasiva de inmunoglobulinas maternas o AG sobre la ocurrencia de diarrea, neumonía y mortali-

dad pre-destete de becerras Holstein.

Resultados principales: Las becerras con TFIP a las 24 h postparto fueron 1.9 más propensas de presentar diarrea pre-destete que las compañeras del hato sin TFIP. Las becerras con AG fueron 2.6 veces más propensas de sufrir diarrea antes del destete que las becerras que no padecían esta afección. Las becerras con TFIP fueron 1.4 veces más propensas de tener neumonía pre-destete que las becerras que no presentaron TFIP. Las becerras con AG tuvieron 2.1 veces más probabilidades de enfermarse de neumonía que las becerras sin AG. Los episodios de diarrea predispusieron a las becerras a enfermarse de neumonía (odds ratio = 3.8). Las probabilidades de morir antes de los 60 días de edad fueron 1.9 veces mayores en las becerras con TFIP comparadas con las becerras sin TFIP.

Aspectos destacados de la investigación: Estos resultados reafirman que TFIP y AG 24 h postparto aumentan el riesgo de diarrea y neumonía pre-destete; además, la diarrea es un factor de riesgo importante de sufrir neumonía. Estas enfermedades solas o coexistentes en las becerras aumentaron notablemente la mortalidad de éstas antes del destete.

Palabras clave: epidemiología, transferencia pasiva, refractómetro, inmunoglobulina, becerras lecheras.

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# Introduction

Feeding practices during the neonatal period significantly impact the success of dairy calf rearing (Godden et al., 2019). Monitoring the quantity of colostral immunoglobulin absorbed following feeding of colostrum by neonatal calves is essential for enhancing the performance and health of preweaning dairy calves (Lopez & Heinrichs, 2022), survival of preweaning calves (Urie et al., 2018) and better performance in later life (Abuelo et al., 2021). An adequate and immediate (within 2 to 3 hafter birth) colostrum supply is vital for establishing passive immunity in calves, and the amount of colostrum fed to newborn calves directly correlates with preventing illness and calf losses (Godden, 2019). Given that colostrum collection and storage practices influence the calf's metabolism, endocrine system, and nutrition (Liermann et al., 2020), it is vital to monitor the quantity, quality, and cleanliness of colostrum and to ensure that newborn calves receive colostrum on time (Fischer et al., 2019).

Because calf diarrhea is one of the most severe problems in dairy farming and a significant cause of economic losses in dairy operations due to high morbidity and mortality rates, high treatment costs, and low growth rate (Elsohaby et al., 2019), the management of colostrum feeding is of particular importance for avoiding this disease (Carter et al., 2021). Likewise, respiratory tract infections resulting in pneumonia are a leading health concern in dairy calves worldwide because this disease has significant consequences for animal welfare, production, antimicrobial use (Jourquin et al., 2023), and lower preweaning weight gain (Cramer & Ollivett, 2019). The appropriate colostral feeding provides better growth and lower occurrence of pneumonia in neonatal calves (Zakian et al., 2023).

Neonatal calves suffering failed transfer of passive immunity (FPI) are more prone to enteric diseases caused by infectious pathogens and pneumonia (Lora et al., 2018). Thus, achieving an optimal transfer of passive immunity in newborn dairy calves is a crucial management goal in dairy farms. Mortality rate is an important indicator of animal welfare and the productivity of a dairy farm (Dawkins, 2017).

Economic losses associated with high mortality include costs incurred by treating and controlling diseases before death, acquiring replacement heifers, and deferred economic loss due to potential genetic loss (Wathes et al., 2008). Additionally, purchasing replacement heifers increases the risk of transmitting diseases in the herd (Torsein et al., 2011). Published data regarding the effect of serum immunoglobulin concentration in neonatal calves on health and mortality are scarce; some have been carried out in beef calves or conducted with limited observations, and some results from earlier studies have been contradictory. These previous findings complicate an accurate estimation of the impact of serum immunoglobulins on preweaning health in dairy calves. Therefore, we hypothesized that the traditional serum immunoglobulins G (IgG) concentration ≥10 g/L, indicative of adequate transfer of passive immunity of colostral immunoglobulins in dairy calves, reduces diarrhea and pneumonia and decreases preweaning mortality of Holstein calves in a high-input dairy operation. This study aimed to determine the effect of serum IgG concentration 24 h postpartum (estimated from serum %Brix) on the occurrence of diarrhea and pneumonia and the mortality of intensively raised Holstein calves.

# Material and methods

#### Animals and management

This project was approved by the Autonomous Agrarian University Antonio Narro Animal Care and Use Committee (#03001-2243). The study was performed on a single large (~3500 milking cows) commercial dairy herd in northeastern Mexico (25°N, elevation 1155 m, mean annual rainfall 228 mm, mean annual temperature 23.8°C) from September 2021 to May 2023. A total of 4,349 female Holstein calves were enrolled in the study.

The farm had a calf-rearing facility with individual outdoor 2.4 m × 1.2 m portable pens with tube sides and plywood roofs with a covered area of 1.6 m<sup>2</sup>. Pens were clean and dry with no bedding (loose-packed soil) and good drainage. Each pen had two feeding pails with holders. Pens were about 0.5 m apart, which minimized microbial loads in the calf ambient. Disinfection of the pens using a high-pressure cleaner and disinfecting afterward was part of the farm routine in the present study. Immediately after birth, calves were separated from their dams, navel-dipped, weighed on a weighing digital scale (Coburn Company, Whitewater, Wisconsin, USA), and raised outdoors in all seasons. Calves were identified using traditional plastic ear tags. Two liters of high-quality colostrum (at least 50 mg/mL of IgG, based on specific gravity reading; JorVet Bovine Colostrometer, Jorgensen Laboratories, Loveland, CO) from freshly calved cows was fed to calves within one hour of birth. Two more liters were given within the next 8 hours of birth. Colostrum was given to all calves by staff members at the dairy herd via esophageal feeders (Nasco, Fort Atkinson, WI).

Calves were offered a milk replacer (MR; 28% crude protein and 20% fat, 4.87 megacalories of metabolizable energy/kg), mastitic milk, and antibiotic milk. MR was reconstituted to 14% solids with warm water and was offered at 0700 and 1430 h daily. The starter grain was a commercial starter containing 23% crude protein and 1.84 megacalories/kg and was offered free choice starting at day 4 of life. Water was offered free choice.

#### Calf health recordings

Employees registered gender and birth weight. Preweaning average daily gain was calculated from birth and weaning weights ( $63.1 \pm 1.9$  days). After birth, the herd veterinarian in charge of calf-raising operations inspects the calves daily and records the occurrence of diarrhea, pneumonia, and calf mortality. Calf diarrhea was defined as loose feces that persisted for two or more days, accompanied by a decreased appetite, lethargy, dehydration (sunken eyes), and fever. Calf pneumonia was diagnosed when the following signs were observed: elevated respiratory rate, serous nasal discharge, coughing, fever, mild depression, and inappetence.

The herd veterinarians treated calves suffering from diarrhea or pneumonia following the standard procedures for these diseases. For pneumonia, treatment was initiated on recognition of inappetence, depression with undifferentiated fever (rectal temperature ≥ 39.4), ear droop, dry cough, and slightly increased respiratory rate. Treatment was based on tulatromycin, bromhexine, and metamizole sodium. Diarrhea was treated when feces were detected on the calf's tail, decreased appetite, lethargy, dehydration, and fever. Treatment was based on marbofloxacin/gentamicin and oral electrolyte solutions. Mortality rate was defined as the number of events during the observation period/total calf days at risk (60). For calves that died, the cause of death was determined according to clinical signs of disease before demise. Calves that died before weaning were censored on the day of death.

#### Assessment of passive immunity

The herd veterinarians collected blood samples (6 mL) 24 h post-calving for serum %Brix determination (serum IgG estimation). Blood samples were collected via jugular venipuncture using a 20-gauge, 1-inch hypodermic needle (BD Vacutainer Precision Glide, Becton Dickinson Co., Franklin Lakes, NJ) into a 10-mL Vacutainer® tube (no anticoagulant; Becton Dickinson, Franklin Lakes, NJ, USA). Blood was allowed to clot at room temperature for approximately one hour and centrifuged at  $2,000 \times g$  for 10 min, and sera was separated within 24 h of collection. Subsequently, the serum was harvested and assayed for %Brix using a digital Brix refractometer (PA202X-003-105, Misco, Cleveland, OH). Calves were categorized as having (serum Brix% < 8) or not having failure of passive immunity (FPI; serum Brix% ≥ 8; equivalent to 10.1 g/L serum IgG, the cut-off point for an FPI positive case, according to equations described by previous studies (Morril et al., 2013; Deelen et al., 2014; Elsohaby et al., 2015) and as having (Brix $\% \le 6.5$ ; equivalent to 0 g/L serum IgG) or not having (Brix% > 6.5) agammaglobulinemia. In the present study, we defined successful passive transfer of antibodies in neonatal calves presenting serum Brix $\% \ge 8$ . However, a detailed updated analysis by Buczinski et al. (2021) shows that the Brix refractometry value for diagnosing adequate transfer of passive immunity in calves is  $\geq 8.4$ . Lombard et al. (2020) indicate that the consensus target Brix measurement for sufficient transfer of passive immunity in calves in the United States is 8.1. To facilitate comparison across previous studies, we defined an adequate TPI status in calves with serum Brix% ≥ 8 because this value is the traditional dairy industry benchmark used in most previously published studies.

#### Statistical analyses

Multivariable logistic regression models were employed to assess the effect of attainment of a BRIX refractometer

**Table 1**. The effect of failure of passive transfer or agammaglobulinemia (based on serum %Brix) on preweaning diarrhea in intensively reared Holstein calves.

Variables	Prevalence, percentage	Odds ratio (OR)1	95% CI (OR)	p
Serum IgG ≤ 10 mg/mL	275/1010 (27.2)	1.8	1.5-2.2	< 0.0001
Serum $IgG > 10 \text{ mg/mL}$	716/3339 (21.4)			
Agammaglobulinemia	110/372 (29.6)	1.9	1.4-2.5	< 0.0001
No agammaglobulinemia	881/3977 (22.2)			

<sup>&</sup>lt;sup>1</sup>Adjusted for season of birth, year of birth, calf's birth weight, and dam parity.

**Table 2**. The effect of a failure of passive transfer or agammaglobulinemia (based on serum %Brix) on the occurrence of preweaning pneumonia in intensively reared Holstein calves.

Variables	Prevalence, percentage	Odds ratio (OR) <sup>1</sup>	95% CI (OR)	р
Serum IgG ≤ 10 mg/mL	169/1010 (16.3)	1.4	1.1-1.7	0.0083
Serum IgG > 10 mg/mL	484/3339 (14.5)			
Agammaglobulinemia	85/372 (22.9)	2.1	1.5-2.9	< 0.0001
No agammaglobulinemia	568/3977 (14.3)			
Occurrence of diarrhea				
Yes	397/991 (40.1)	3.8	3.1-4.8	< 0.0001
No	256/3358 (7.6)			

<sup>&</sup>lt;sup>1</sup>Adjusted for season of birth, year of birth, calf's birth weight, and dam parity.

**Table 3**. Mortality outcome of Holstein calves with failure of passive transfer or agammaglobulinemia as diagnosed by serum %Brix.

Variables	Prevalence, percentage	Odds ratio (OR)1	95% CI (OR)	p
Serum IgG ≤ 10 mg/mL	76/1010 (7.5)	1.9	1.4-2.7	0.0002
Serum IgG > 10 mg/mL	137/3339 (4.1)			
Agammaglobulinemia	44/372 (11.9)	2.6	1.6-4.0	< 0.0001
No agammaglobulinemia	169/3977 (4.3)			
Preweaning mortality with occurrence of diarrhea				
Yes	120/991 (12.1)	2.4	1.7-3.4	< 0.0001
No	93/3358 (2.8)			
Preweaning mortality with occurrence of pneumonia				
No	119/3696 (3.2)	0.4	0.4-0.5	< 0.0001
Yes	94/653 (14.4)			
Preweaning comorbidity pneumonia and diarrhea				
Yes	65/414 (15.7)	2.3	1.6-3.6	< 0.0001
No	148/3935 (3.8)			

<sup>&</sup>lt;sup>1</sup>Adjusted for season of birth, calf's birth weight, year of birth, and dam parity.

reading  $\geq 8$  (serum IgG  $\geq 10.1$  g/L) 24 h after birth and the occurrence of agammaglobulinemia 24 h after birth on the incidence of preweaning diarrhea and pneumonia, as well as mortality of calves (response variables), using the maximum likelihood method of the LOGISTIC procedure of SAS (SAS Institute Inc., Cary, NC; version 9.4). The general equation of the logistic regression model was defined as follows: Logit  $(\pi) = \alpha + \beta_1 X_1 + \beta 2 X_2 + ... + \beta_n X_n$ 

Where  $\pi$  was the probability of diarrhea, pneumonia, and death;  $\alpha$  was the intercept parameter;  $\beta_1$  to  $\beta_n$  were the logistic regression coefficients (parameter estimates) for the explanatory effects ( $X_1$  to  $X_n$ ) included in the statistical model. No elimination method was used to remove variables from the model because a standard view in epidemiology is that automated confounder selection methods, such as backward elimination, should be avoided as they can lead to biased effect estimates and underestimating their variance. The strength of the associations was estimated using adjusted odds ratios and the 95% confidence interval (95% CI).

Each multivariable model included potential confounders such as birth weight, season of birth, year of birth, dam parity, and gender. Birth weight was categorized as lower or greater than 37 kg. Parity was grouped into three categories: 1, 2-3, and >3. December, January, and February were grouped as winter; March, April, and May as spring; June, July, and August as summer; and September, October, and November as autumn. The Hosmer and Lemeshow chisquared goodness-of-fit test was used to assess the whole fitness of the logistic regression model. A histogram for serum IgG based on BRIX refractometer reading was prepared with the Statgraphics Centurion XV software (Statpoint Technologies Inc., Warrenton, VA, USA). For the time of disease (pneumonia or diarrhea) occurrence postpartum, survival analyses were performed for calves with FPI or not FPI, using the Cox proportional hazard model (Statgraphics Centurion XV software). Interval from birth to disease occurrence was the dependent variable. Survival curves were generated at an exit time point of 60 days (weaning). For all the analyses, the significance was established at p < 0.05.

#### Results

Of the 4,349 calves born alive and included in the study, 22.8% had diarrhea (n = 991), and 15.0% had pneumonia (n = 653) in the preweaning period. The mean age of calves with diarrhea was  $10.5 \pm 6.6$  d, while for calves with pneumonia, it was  $39.1 \pm 16.4$  d. The overall calf mortality was 4.9 per 100-calf 60-days at risk. The majority of deaths occurred in calves less than 55 days of age, with an average age of 27 days. Serum IgG (estimated from equations of Morrill et al., 2013; Deelen et al., 2014; and Elsohaby et al., 2015) in calves 24 h postpartum ranged from 0.0 to 44.4 g/L. Calves with reduced absorption of maternal immunoglobulins (hypogammaglobulinemia; <10 g/L IgG) was 19.0%, whereas the percentage of calves

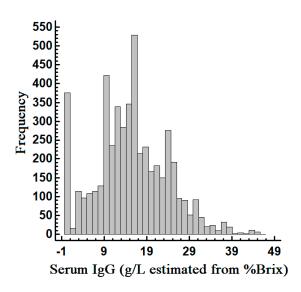
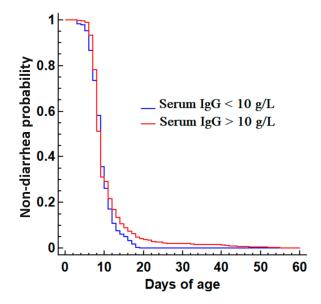


Fig. 1. Histogram of the distribution of serum IgG concentrations 24 hours after birth for 4,349 Holstein calves, estimated from %Brix.



**Fig.** 2. Kaplan-Meier curves for 991 Holstein calves with adequate serum levels of IgG (%Brix 8.0 equivalent to  $\geq 10.1$  g/L) or failure of passive transfer (Brix%  $\leq$  8; equivalent to  $\leq$ 10 g/L serum IgG) at 24 hours post calving, depicting non-diarrhea probability at 60 days post-calving.

with agammaglobulinemia (AG) 24 h after birth was 7.4%. The histogram describing the frequency of serum IgG concentrations in calves exhibited a positively skewed distribution with a mean ( $\pm$  SD) of 15.4  $\pm$  8.5 (Fig. 1), which indicated that most IgG concentrations felt into the fair to excellent range (Lombard et al., 2020).

Calves that did not attain adequate serum IgG levels (≤ 10 g/L) had higher odds for diarrhea during the preweaning period than calves with FPI (Table 1). AG calves 24 h post-calving had higher odds for diarrhea than calves with no AG. Calves with FPI were more likely to suffer pneumonia than calves with adequate serum IgG concentration 24 h postpartum (Table 2). Compared to all calves not having

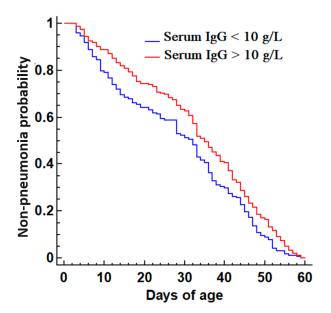


Fig. 3. Kaplan-Meier curves for 653 Holstein calves depicting non-pneumonia probability in animals with adequate serum IgG levels, (%Brix 8.0 equivalent to  $\geq 10.1$  g/L) or failure of passive transfer (Brix%  $\leq$  8; equivalent to  $\leq$ 10 g/L serum IgG) at 60 days post calving.

AG, AG calves 24 h post-calving were 2.1 times more likely to have pneumonia.

Compared to calves with adequate serum IgG 24 h post-calving, calves with FPI were 1.9 times more likely to die before weaning (Table 3). Calves with AG 24 h post-calving had twice the risk of dying than those with no AG. The occurrence of diarrhea greatly affected the mortality rate of calves; likewise, the absence of pneumonia had a protective effect on mortality rate of calves. The odds of mortality were 2.3 times higher in calves with comorbidity of diarrhea and pneumonia compared with calves without these diseases (Table 3).

Kaplan-Meier survival curves for calves suffering diarrhea or pneumonia at 60 exit points by serum IgG concentration at 24 h of life are represented in Fig. 2 and Fig. 3, respectively. The survival curve for diarrhea illustrates that most reported clinical signs occurred at around 10 days postpartum and then tapered off for the rest of the preweaning period. In the case of the survival curve for pneumonia, most of the cases occurred at around 30 days with no tapering off for the rest of the preweaning period and with a clear difference for calves with FPI and adequate serum IgG in one-day-old calves.

## **Discussion**

Comparisons of the prevalence of FPI among studies in dairy calves are complicated due to variations in weather conditions, differences in rearing management, colostrum administration, and serum total proteins or IgG concentration used as the threshold for distinguishing calves with and without FPI. Even so, similar to previous studies (Staněk et al., 2019), this study shows that the

transfer of passive maternal immunity in intensively raised calves is a significant problem.

Similar to findings of Al-Alo et al. (2018), where newborn calves with higher serum IgG levels had a reduced risk for diarrhea compared with calves with lower serum IgG, in the present study, calves with FPI or GA had a higher risk for the occurrence of this enteric disease. However, other studies have not found an association between passive immunity status and diarrhea (Raboisson et al., 2016; Schinwald et al., 2022). This discrepancy may arise from different methodologies to measure IgG, dissimilar populations, or environmental variations among studies.

Failed transfer of passive immunity seems responsible for a higher incidence of enteric diseases, increased use of antibiotics in calves, and, consequently, longer rearing periods, constituting a public health, economic, and animal welfare issue. Calves with passive immunity mount a protective immune response against pathogenic agents causing diarrhea in neonatal calves (Ridpath et al., 2003). Thus, these results reaffirm that to protect calves against enteric pathogens, newborn animals should absorb adequate amounts of immunoglobulins from colostrum (Gulliksen et al., 2009).

Calves in the present study did not have an etiological work-up. At least ten primary enteric pathogens are involved in calf diarrhea (Cho & Yoon, 2014). The only infectious agent previously identified in the studied site is *Cryptosporidium parvum* (Delgado-González et al., 2019). A negative correlation has been shown between the passive transfer of anti-*C. parvum* IgG antibody via colostrum during the first 24 h of life and the detection of cryptosporidiosis early in life in calves (Wang et al., 2003; Lefkaditis et al., 2020). However, in the present study, other pathogens implicated in calf diarrhea and the sources of infections are unknown. These findings suggest that colostral antibodies partially protect newborn calves during their first day of life and highlight the importance of colostrum absorption in preventing neonatal diarrhea.

One of the main focuses of this study was to examine the association between post-colostral serum IgG levels of calves and preweaning pneumonia. In this study, inadequate serum IgG levels in calves increased the risk for cliniciandiagnosed pneumonia, which is in line with previous studies where high blood levels of colostrum-derived IgG in calves are associated with reduced risks of this disease in dairy calves (Virtala et al., 1999; Sutter et al., 2023). However, other studies found a lack of association between serum IgG and the occurrence of pneumonia in dairy (Pithua and Aly, 2013) and beef (Waldner & Rosengren, 2009) calves. This discrepancy could be due to various factors such as the quality of records kept by producers, stress, hygiene management, colostrum quality, quantity, and feeding time. IgG is effective in defense of the bovine respiratory tract against pathogenic microorganisms by opsonizing for enhanced recognition by macrophages and neutrophils, activating complement, blocking colonization sites, and neutralizing bacterial toxins (Caswell, 2014). Thus, detecting hypogammaglobulinemia in 24-hourold calves could hint at developing better management practices to diminish pneumonia in pre-weaned dairy calves.

In the present study, calves that survived diarrhea during the preweaning period were more susceptible to pneumonia before weaning, which agrees with previous reports that demonstrated the importance of diarrhea as a risk factor for the occurrence of pneumonia (Virtala et al., 1999; Taylor et al., 2010; Gomes et al., 2021). A calf's susceptibility to pneumonia is influenced by the strength of its immune system and a previous occurrence of diarrhea (Ackermann et al., 2010). The way diarrhea predisposes the occurrence of pneumonia could be due to nutritional setbacks that could deplete body fat, compromising the immune system and thus leaving the calf susceptible to subsequent respiratory infection (Moore et al., 2002). Also, diarrhea alters the gut microbiota, resulting in dysfunction of the gastrointestinal tract (Oultram et al., 2015; Van Vleck Pereira et al., 2016), which increases the risk for pneumonia. Another possibility could be that some pathogen agents, such as bovine coronaviruses, are associated with both neonatal calf diarrhea and pneumonia (Vlasova & Saif, 2021); furthermore, in cases with severe debilitation, exists the possibility of complicating conditions such as bacterial pneumonia (Peek et al., 2018).

The current study established that calves with FPI or suffering AG had greater odds of dying before weaning. These results align with other studies indicating that calves with serum total proteins <5.0 were 2.4 times more likely to experience mortality than those with serum total protein ranging between 5.0 and 6.0 g/dl (McCorquodale et al., 2013). Stilwell & Carvalho (2011) showed that mortality due to infectious diseases was higher in the group with plasma IgG <10 mg/mL. Crannell & Abuelo (2023) found that preweaning mortality risk was higher in calves with poor passive immunity transfer than in excellent passive immunity. However, other studies have shown that serum IgG concentration has not resulted in a significant predictor of hazard for mortality (Chigerwe et al., 2015). It is worth noting that some studies have only evaluated serum total protein concentrations and not serum IgG concentrations to assess passive immunity. Still, IgG determination is considered the reference method for determining passive transfer because the correlation between total proteins and serum IgG concentrations is inconsistent (Wilm et al., 2018). Thus, the present study reaffirms that FPI in neonatal calves is responsible for reduced resistance to disease and increased mortality in calves early in life.

In line with other studies in different environments, despite the antimicrobial therapy, comorbidity of diarrhea and pneumonia markedly increased the risk of calf mortality (Gulliksen et al., 2009; Alemu et al., 2022; Schinwald et al., 2022). These results are partly due to nutrient malabsorption, electrolyte loss, and respiratory tract lesions (Gaudino et al., 2022).

It was concluded that low post-colostral IgG levels and agammaglobulinemia were significant risk factors for pneumonia and diarrhea in the preweaning period. Also, calves with diarrhea faced an increased chance of pneumonia. Calves diagnosed either with diarrhea or pneumonia had a significantly increased risk of death. This study indicates that to reduce calf mortality in high-input dairy farms, attention should be focused on monitoring serum IgG 24 h postpartum in calves to ensure the attainment of adequate colostral-derived immunoglobulins. Also, the present study suggested that a digital Brix refractometer represents a valuable tool for estimating serum IgG in calves on time and for evaluating the success of the colostrum feeding program.

**Competing interests:** The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

**Ethical approval:** The Autonomous Agrarian University Antonio Narro Institutional Animal Care and Use Committee approved all actions connected with cows used for this study (protocol number 3001-2114).

Authors'contributions: Mely T. Olivera: Data curation, Investigation. Jesús Mellado: Funding acquisition. José E. García: Data curation. Juan A. Encina: Validation, Visualization, Writing – review & editing. Perpetuo Álvarez: Methodology, Visualization, Writing – review & editing. Ulises Macías-Cruz: Investigation. Leonel Avendaño: Formal analysis. Miguel Mellado: Conceptualization, Formal análisis, Funding acquisition, Project administration, Supervision, Writing – original draft.

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