A Cohort Study of the Association Between Serum Immunoglobulin G Concentration and Preweaning Health, Growth, and Survival in Holstein Calves

P. Pithua [a]*

S.S. Aly [b]

[a] *Department of Veterinary Medicine and Surgery, University of Missouri, Columbia, MO 65211*

[b] *Department of Population Health and Reproduction, University of California, Davis CA 95616*

[c] *Veterinary Medicine Teaching and Research Center, School of Veterinary Medicine, University of California Davis, Tulare CA 93274*

**Corresponding author. Tel.: +15734894389*
E-mail address: pithuap@missouri.edu (P. Pithua).

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ABSTRACT

The association between serum IgG concentration and preweaning health performance in Holstein calves were evaluated in a prospective cohort study design framework. Post colostral blood samples were collected from 561 calves and serum IgG concentrations were quantitated using a single radial immunodiffusion assay. Preweaning treatments for diarrhea, pneumonia, omphalitis and frequency of antibiotic therapy plus calf death events were recorded until calves were weaned at approximately 60 d of age. Logistic regression modeling was used to evaluate the association between failure of passive transfer of immunity (FPT, serum IgG < 10g/L) and risk of diarrhea, pneumonia, omphalitis, frequency of antibiotic therapy and death. Calves with FPT were twice as likely to suffer from scours (OR = 2.34; 95% CI = 1.54 to 3.56), otitis media (OR = 2.62; 95% CI = 1.28 to 5.35) and be treated with antibiotics (OR = 2.20; 95% CI = 1.55 to 3.12) during the preweaning period as herd mates that had adequate passive transfer of immunity (APT, serum IgG ≥ 10 g/L). Although FPT status was not associated with pneumonia, omphalitis, and preweaning mortality risks in this study, mean preweaning daily live weight gain (kg/d) was significantly lower for calves with FPT relative to calves with APT.

INTRODUCTION

Intake of colostrum by a calf soon after its birth is considered critical for its growth and survival during the preweaning period. Natural maternal colostrum is a rich source of essential nutrients and contains absorbable immunoglobulin (IgG) that provides a first line of defense against pathogens present in the calf's environment. [1] Feeding poor quality or complete lack of intake of MC by a calf is a well-recognized risk factor for failure of passive transfer of immunity

(FPT), a condition generally defined by serum IgG levels ≤10 g/L in calves. [2]

Failure of passive transfer is prevalent in calves on many US dairy operations with recent estimates by USDA's National Animal Health Monitoring System indicating that at least 19% of dairy heifer calves in US herds suffered from FPT in 2007, with risks increasing for calves born in herds that feed pooled colostrum, allowed natural nursing, and hand fed colostrum ≥ 4 h after birth. [3] While FPT is not a disease, the condition has been linked with poor preweaning calf performance in several studies that utilized serum total proteins (TP) as a proxy measure for serum IgG concentration.[4-6]These studies were motivated by findings showing high correlations between TP and serum IgG concentrations. [5] However, use of TP as a marker for serum IgG concentrations presents a number of limitations. First, correlation between TP and serum IgG concentrations does not necessarily equate to causation. Additionally, refractometry, the primary method of determining TP levels in serum specimens is subjective providing an unreliable qualitative measure for TP. [5, 7, 8] Studies [4-6] that used serum TP as a proxy for serum IgG concentrations were likely prone to misclassification of FPT status of calves leading to biased estimates of the association between FPT and calf health outcomes. Moreover, the perceived correlation between serum TP and IgG while shown to be high in some studies, [5, 9] remains an imperfect correlation. Further, in calves fed commercial colostrum replacer, the TP cut points predictive of adequate transfer of immunity (serum IgG ≥ 10 g/L) likely varies depending on what type of the colostrum replacement product is fed.

Few studies have addressed the question of the effect of FPT, as measured by serum IgG concentrations on health and performance outcomes in dairy calves during the preweaning period. In one such study, FPT (defined as serum IgG < 12 g/L) was associated with decreased growth rates and daily weight gains plus increased morbidity and mortality risks in calves up to six months of age.[10] However, a limitation of that study was that the effect of FPT (defined as serum IgG < 12 g/L) on morbidity, and survival was evaluated in a 1000 calves that originated from a single Arizona dairy herd and raised offsite. Thus, while internally valid, it was impossible to extrapolate the findings of that study[10] to other dairy herds in the US, and in herds with differing management systems, given the lack of representation to the wider population of dairy herds. In beef cattle, studies looking into variations of this question have mostly yielded conflicting findings. For example, while two previous studies found no association between FPT (defined here as serum IgG1< 2400 mg/dL and serum IgG1< 24 g/L, respectively) and calf treatment for diarrhea, pneumonia, omphalitis, or treatment for any reason,[11, 12] a separate study[13] found a significant association between low IgG concentrations and higher morbidity and mortality rates plus a decrease average daily weight gain (ADG). The objective of the present study was to describe the association between serum IgG concentrations measured at 24 h post-colostral intake and preweaning health performance in Holstein calves. Specifically, the preweaning risks of treatments for diarrhea, pneumonia, omphalitis, otitis, and antibiotic treatments were evaluated for calves with a history of FPT (serum IgG < 10 g/L) compared to calves with adequate passive transfer of colostral immunity(serum IgG ≥ 10 g/L). Associations of FPT with average daily live weight gain (ADG) and preweaning calf mortality risks were also described.

MATERIALS AND METHODS

Experimental Design and Herd Selection

In this study, data collected in a previous field trial[14] performed to evaluate the effect of feeding a commercial lacteal-derived colostrum replacer (CR) on measures of FPT, and preweaning health performance was secondarily analyzed in a prospective cohort study design framework. The original study was performed in a California Holstein dairy that milked 3,600 cows and routinely fed raw pooled-MC to calves. The herd was selected because of its large size (≥ 3,600 cows), maintenance of electronic records through participation in the California DHIA milk testing program, and a willingness of the owner to comply with the study protocols.

Colostrum Feeding Protocols and Calf Management

Calves were enrolled in the original study [14] between September and December, 2010. Pregnant cows were transferred to a group calving pen within 24-72 h of the expected calving date and monitored until calving. Heifer calves were separated from their dams within 6 h of birth and denied the opportunity to suckle their dam or other cows in the pen whenever possible.

Random permuted blocks were used to generate a pre-randomized list that was sealed with opaque sticky notes. Using these random lists that was sequentially unsealed to reveal the treatment group, calves were assigned to be fed either 3.8 L of pooled-MC (control group, n = 273) or two packages of a lacteal-derived CR[a] (treatment group, n = 295) reconstituted per the manufacturer's instructions. Each package containing 100 g IgG of the lacteal-derived CR powder was dissolved in 1 L of warm water (approx. 49^{o}C) yielding a mixture of 1.4 L containing 71.4 g/L of IgG. The pooled-MC fed was typically harvested from between 5 to 10 cows within 1 to 12 h of calving, mixed together in a bulk tank and refrigerated at 4^{o}C until feeding, often within 6-12 h of collection. Both the lacteal-derived CR and pooled-MC were administered as a single oral dose (CR ~ 2.8 L and MC ~3.8 L) within 6 h of birth. All calves were fed using a bottle nipple. However, when a calf failed to suckle some quantity of the assigned colostrum, an esophageal tube feeder was used to deliver the remaining volume of colostrum.

During this period, calves were maintained on recommended calf diets including milk replacer, calf starter grain, and free choice fresh water. Each calf was housed in an individual wooden hutch until weaning at approximately 60 d of age.

Sample Collection and Processing

Blood samples were collected using 10 mL plain tubes[b] from each calf through jugular venipuncture prior to and after 24 h of colostrum intake. The blood samples were centrifuged for five minutes at 1,000 g to harvest serum. Next, IgG (g/L) concentrations in sera samples were quantified using a radial immunoassay as described.[15, 16]

Data collection and calf health monitoring

Upon enrolment, each calf was identified with an ear tag, weighed at birth and later at weaning at approximately 60 d old. Other records included the dam's identification, treatment group (lacteal-derived CR or pooled-MC), birth date, duration to separation from the dam (h), duration to feeding colostrum (h), quantity of colostrum fed (L) and whether or not an esophageal tube feeder was used.

Preweaning calf disease incidence were monitored by research assistants who documented treatments for diarrhea, pneumonia, omphalitis (i.e. navel ill or joint illness), frequency of antibiotic therapy, and whether or not; a calf died or was successfully weaned at the end of the study period (approximately 60 d old). Disease monitoring assistants were masked to the type of colostrum (lacteal-derived CR or pooled-MC) each calf received at birth. Before the study onset, the assistants received standard training in identifying the common calf hood disease events of interest to limit the possibility of subjective evaluation of disease outcomes.

Disease monitoring involved checking each calf at feeding for symptoms of depression, low appetite, abnormal fecal consistency, increased respiratory rate, cough, nasal and ocular discharges plus other gross abnormalities in the calf's demeanor. When necessary, the joints were physically examined for heat, swelling and abnormal gait. Navels were examined for evidence of inflammation, including swellings or abnormal discharges. A calf displaying these symptoms was examined further by measuring the rectal temperature to determine whether they were hypothermic additional to complete assessment of fecal consistency and hydration status.

In this study, a disease event was recorded only once for each calf although some calves were treated for multiple episodes of the same disease. Calves were monitored from birth until approximately 60 d old for disease symptoms at which point they were censored from the study. Calves that died prior to weaning were censored at their date of death. No specific treatment protocols were developed for this study. Instead, the herd relied on their regular veterinarian for advice on treatment decisions for sick calves. However, diagnoses recorded by the study assistants were validated using the herd Veterinarian's formal diagnosis and treatment records.

Case definitions for calf disease events

To limit subjectivity in personnel recorded diagnosis, the following working definitions were applied in this study: (a) diarrhea (i.e. scours) was indicated in calves that voided abnormal feces with watery consistency and foul smell with or without dehydration or elevated body temperature (≥ 40 ^{o}C), (b) respiratory disease was reported for calves that exhibited increased respiratory rate, nasal discharges, or cough with or without an elevated body temperature (≥ 40 ^{o}C), (c) omphalitis (navel infections) was associated with presence of overt umbilical inflammatory signs, including heat, swelling, purulent discharges, or evidence of pain on palpation of the umbilical area, and (d) droopy ears and a head tilt to the side of the ear droop was indicative of otitis media.

Definition of study cohorts

The calves with FPT indicated by serum IgG levels <10 g/L at approximately 24 h of age were considered at risk, and defined as the 'exposed' group. Calves with adequate passive transfer of IgG (APT), indicated by serum IgG levels ≥10 g/L at 24 h old was considered less at risk and defined as the 'unexposed' group.[2]

Data analysis

The primary outcomes in this study were risk of respiratory disease (yes/no), diarrhea (yes/no), omphalitis (yes/no), otitis media (yes/no),treatment with antibiotics (yes/no), calf death risk within 60 d of birth (yes/no), and ADG.

The association between FPT (serum IgG < 10 g/L vs. ≥ 10 g/L) and risk of treatments for pneumonia, diarrhea, omphalitis, otitis media, treatment with antibiotics, and calf deaths within 60 d of birth was each evaluated by fitting a univariate logistic regression model to the data. Fit of the data to each model was evaluated using Hosmer-Lemeshow Goodness-of-fit test. [17]

Daily weight gain for each calf was calculated by dividing the difference between weaning and birth weight (kg) with age of the calf at weaning (d). Next, mean± SD for ADG was calculated and the difference between cohorts (serum IgG < 10 g/L vs. ≥ 10 g/L) evaluated using the student's t-test. Finally, a simple least-squares regression model was fitted to the data to evaluate the association between FPT (serum IgG < 10 g/L vs. ≥ 10 g/L) and ADG. Data was analyzed using Stata software version 12[c] and a value of P ≤ .05 was indicative of statistical significance.

RESULTS

Five hundred and sixty-one calf records were available for analysis. Of these, 222 (40%) were calves that experienced a FPT (serum IgG < 10 g/L) event while the remaining 339 (60) had an adequate passive transfer of immunity within 24 h of colostrum intake. Twenty-four percent (54/222) of calves with FPT were treated for pneumonia compared with 20% (67/339) of herd mates without FPT. Diarrhea was observed in 29% (64/222) of calves with FPT compared with 15% of calves with APT. The risk of omphalitis was less than 1% in both exposed (FPT, serum IgG < 10 g/L) and unexposed (FPT, serum IgG≥ 10 g/L) groups of calves while the proportion of calves treated for otitis media was significantly higher in calves with FPT compared with calves with APT(9%, 21/222 vs. 4%, 13/339). Overall,

Table 1. *Final logistic regression models of the relationship between failure of passive transfer in calves and preweaning risk of morbidity and mortality.*

					95% Conf.	
Predictor	Level	N	% treated	OR	Interval	*P*
Pneumonia						
FPT, serum IgG < 10g/L	Yes	222	24	1.31	0.87 to 1.96	0.2
	No	339	20	Ref.	–	–
Scours						
FPT, serum IgG < 10g/L	Yes	222	29	2.34	1.54 to3.56	<0.001
	No	339	15	Ref.	–	–
Omphalitis						
FPT, serum IgG < 10g/L	Yes	222	0.45	1.53	0.1 to 24.5	0.76
	No	339	0.29	Ref.	–	–
Otitis media						
FPT, serum IgG < 10g/L	Yes	222	9	2.62	1.28 to 5.35	0.008
	No	339	4	Ref.	–	–
All treatments with antibiotics						
FPT, serum IgG < 10g/L	Yes	222	50	2.20	1.55 to 3.12	<0.001
	No	339	31	Ref.	–	–
Calf death						
FPT, serum IgG < 10g/L	Yes	222	11	0.81	0.48 to 1.36	0.42
	No	339	14	Ref.	–	–

50% (111/222) of calves with FPT were treated at least once with antibiotics during the preweaning period compared with 31% (106/339) of calves with APT. Mean daily live weight gain (kg/d) was significantly higher (student's t-test P < 0.0001) among calves with APT (mean ± SD (n); 0.41 ± 0.14 (319)) compared with herd mates who experienced FPT (mean ± SD(n); 0.33 ± 0.14 (199)). Calf death risk among calves with FPT was 11% (25/222) compared with 14% (46/339) in calves with APT.

In this study, calves with FPT were at least twice as likely to suffer from diarrhea (OR = 2.34; 95% CI = 1.54 to 3.56), otitis media (OR = 2.62; 95% CI = 1.28 to 5.35), and be treated with antibiotics (OR = 2.20; 95% CI = 1.55 to 3.12), during the preweaning period as herd mates who had APT (Table 1). Further, although FPT status was not associated with pneumonia, omphalitis, and preweaning calf death risks, mean preweaning daily weight gain (kg/d) was 0.076 lower among calves with FPT relative to calves with APT (Table 1).

DISCUSSION

Preweaning daily live weight gain

The overall finding in this analysis of a significant increase in ADG associated with APT (serum IgG ≥ 10 g/L vs. < 10 g/L) is similar to observations in a previous study in which higher concentrations of serum IgG at 24 to 48 h was linked with an increase in ADG during the preweaning period in dairy calves[10]. It seems plausible that better feed intake plus efficient dry matter utilization resulting from a superior preweaning health in calves with APT was a likely reason for the increase in ADG observed in this study[1] although other studies have found no significant association between disease and ADG[18]. An earlier evaluation of a similar question in feedlot cattle revealed no significant relationship between serum IgG concentration and ADG.[19]

Preweaning morbidity risks

In this study, FPT was not associated with preweaning risks of pneumonia and omphalitis. These results, while consistent with findings from an earlier study in which a lack of association between serum IgG concentrations and specific treatments for pneumonia and omphalitis was reported in Beef calves[12], differed from another study which found a significant association between low postcolostral serum IgG levels and development of pneumonia in diary calves. [20] Further, although calves with FPT were twice as likely to suffer from diarrhea as herd mates with APT in the present study, this finding differed from studies reporting no associations between serum IgG concentrations and risk of treatment for diarrhea. [11, 12]

Preweaning health is a function of several factors, which include the reduction in exposure of new-born calves to putative risk factors (infectious agents inclusive) through proper housing, ventilation, and general hygiene; increasing levels of specific and non-specific immunity through provision of good-quality colostrum, balanced nutrition, stress minimization; and boosting specific resistance through preventive vaccinations of either the dams or new-born calves against specific pathogens.[21, 22]Therefore, whether a calf suffers from a preweaning morbidity event has to be weighed against its immune status and the pathogen exposure risk present in the environment. [21] It is possible that calves may still experience a preweaning morbidity incident despite APT or be protected against common calf hood diseases in spite of FPT. [1, 21] The calves in the current study were housed in individual wooden hutches up to 60 d of age and maintained on preweaning diets of milk replacer, calf starter grain, and fresh water ad libitum. Although several calf management practices were in place to limit exposure to risk factors for disease in the study herd, it is entirely possible that some yet unidentified factor(s) unrelated to FPT may have contributed to the additional risk of diarrhea (e.g. compromised sanitation protocols) or otitis (e.g. higher within-herd Mycoplasma sp. challenge) leading to the increased antibiotic usage observed in the study herd. Low serum IgG concentrations were associated with increased preweaning risks for otitis media in this study. This finding was likely a consequence of a higher within-herd *Mycoplasma* species challenge, [23] although this theory could not be further verified given that samples were not tested to confirm a possible etiological role of this pathogen in the development of otitis media in the study calves due to budget limitations.

Preweaning calf death risk

Even though the lack of association between FPT and preweaning calf death risk in this study was consistent with findings reported elsewhere,[12] an earlier study in dairy calves found a significant association between serum IgG concentration (serum IgG <12 vs.≥ 12 mg/ml within 24 h) and increased calf death risks during the preweaning period[10]. These contradictory findings underscore the fact that, calf mortality risks, like morbidity, is a function of several factors and that other management factors, including housing and nutrition in concert with adequate colostral immunity is essential for calf survival during the preweaning period. [1, 21, 22]

CONCLUSIONS

The goal of this study was to describe the association between serum IgG concentrations and preweaning health performance in Holstein calves. The risk of treatment for diarrhea and otitis media was significantly higher among calves with FPT. Even though there were no differences in preweaning risks for pneumonia, omphalitis and death risk in calves with FPT compared with herd mates with APT, the ADG was significantly higher for calves with APT (vs. FPT). Findings reported here must be interpreted with caution due to some limitations. First, the associations reported here do not confirm a cause-and-effect relationship because of the observational nature of the study design employed. Second, usage of a single herd to evaluate study objectives undermined the ability to extrapolate the current results to a wider population of dairy herds. Third, our study was restricted to calf health and survival outcomes observed only during the preweaning period (i.e. up to 60 d of age). As such, the potential effects of FPT on calf health and performance in the post weaning period were not evaluated. Regardless, the increased risk of treatments for diarrhea and otitis media, plus the low ADG associated with FPT identified in this study imply that producers should remain vigilant and pursue strategies that minimize the risk of FPT starting with best colostrum harvesting, storage, and feeding management practices. [24-26]

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CONFLICTS OF INTEREST

None

a. Land O Lakes Colostrum Replacement, Lake O Lakes Animal Milk Products

b. Becton, Dickinson and Co., Franklin Lakes, NJ

c. Stata® Corp., College Station, TX, USA

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