DOI: 10.1002/vms3.1006

ORIGINAL ARTICLE

WILEY

Characteristics of Holstein cows predisposed to ketosis during the post-partum transition period

Seungmin Ha[1] | Seogjin Kang[1] | Mooyoung Jeong[1] | Manhye Han[1] | Jihwan Lee[1] | Hakjae Chung[1] | Jinho Park[2]

[1]Department of Animal Resource Development, Dairy Science Division, National Institute of Animal Science, Rural Development Administration, Cheonan, Korea

[2]College of Veterinary Medicine, Jeonbuk National University, Iksan, Republic of Korea

Correspondence
Jinho Park, College of Veterinary Medicine, Jeonbuk National University, Iksan 54596, Republic of Korea.
Email: jpark@jbnu.ac.kr

Funding information
The improvement of animal diseases control in National Institute of Animal Science, Grant/Award Number: PJ01567603; National Institute of Animal Science, Rural Development Administration, Republic of Korea

Abstract

Background: Ketosis is a common metabolic disorder during the post-partum transition period of dairy cattle. How the method of reproduction, parturition time, and calf birth weight affect the occurrence of ketosis on dairy herds remains elusive.

Objectives: This study investigated factors associated with the severity of ketosis.

Methods: We divided 186 Holstein cows into three classifications based on the highest β-hydroxybutyrate (BHBA) concentration during the post-partum transition period, namely non-ketosis (<1.2 mmol/L, $n = 94$), subclinical ketosis (1.2–2.9 mmol/L, $n = 58$), and clinical ketosis (≥3.0 mmol/L, $n = 34$). We evaluated characteristics of cows associated with the severity of ketosis.

Results: Ketosis was not associated with the method of reproduction, parturition time, pregnancy wastage, premature delivery, retained placenta, and type of calf. Cows calving in spring and especially summer were at higher risk of severe ketosis ($p < 0.01$). Cows with increased body condition score (BCS) at parturition, age, lactation number, and calving interval were more likely to develop severe ketosis ($p < 0.05$). Cows with clinical ketosis produced most milk (29.9 ± 1.0 kg) from days four to six, whereas cows without ketosis produced the least (21.3 ± 0.8 kg) ($p < 0.001$). Heavier calf birth weight resulted in high risk of severe ketosis ($p < 0.01$), due to increased milk yield during the early lactation.

Conclusions: The severity of ketosis is associated with the calving season, BCS at parturition, age, lactation number, calving interval, milk yield in the early lactation period, and calf birth weight. Nonetheless, it was not associated with the method of reproduction, parturition time, pregnancy wastage, premature delivery, retained placenta, and type of calf. This study is the first to investigate the associations between ketosis and calf birth weight. Our findings could help predict cows at risk of ketosis and take precautions.

KEYWORDS
ketosis, characteristics, Holstein cows, transition period

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.
© 2022 The Authors. *Veterinary Medicine and Science* published by John Wiley & Sons Ltd.

1 | INTRODUCTION

Ketosis is a common metabolic disease during the post-partum transition period in dairy cows with high yield. It has various manifestations, namely inappetence, decreased milk yield, loss of body weight, preference of forages to concentrate, dry manure, fruity odour in breath or milk, prostration, and nervous signs, including vigorous licking and aggressive behaviour (Duffield, 2000; Berge & Vertenten, 2014; Dar et al., 2018; Guliński, 2021; Lei & Simões, 2021). Ketosis exerts an economic impact on the dairy farming industry, which involves treatment, decreased milk production, increased risk of developing displaced abomasum, metritis, lameness, reproductive performance, and culling (LeBlanc et al., 2005; Walsh et al., 2007; McArt et al., 2012; Suthar et al., 2013). The cost per case of ketosis per year varies. In the United States, the total cost ranged from US$129 to US$289 (McArt et al., 2015; Liang et al., 2017). In Europe, costs of subclinical ketosis ranged between €130 and €257 (Raboisson et al., 2015; Mostert et al., 2018). The costs of clinical ketosis are approximately 4.7 times higher than those of subclinical ketosis (Steeneveld et al., 2020). Other concurrent diseases commonly associated with ketosis double these costs (Benedet et al., 2019).

Researchers have investigated techniques of predicting ketosis, using haematological, serum biochemical, and genetic analysis, besides automatic monitoring system and machine learning (Sun et al., 2015; Belay et al., 2017, Cocco et al., 2021; Satoła & Bauer, 2021; Ha et al., 2022). However, it is difficult to apply these techniques to all dairy farms owing to economics. Several publications have documented the characteristics of dairy cows susceptible to ketosis worldwide. The incidence of ketosis is affected by the surroundings as well as the status of the animal (Suthar et al., 2013; Berge & Vertenten, 2014; Brunner et al., 2019). The body condition score (BCS), lactation number, calving season, prolonged previous lactation length, 305-day milk yield and the average milk protein percentage in the previous lactation, increased colostral production, milk fever, and retained placenta have been associated with ketosis in European dairy farms (Rasmussent et al., 1999; Berge & Vertenten, 2014; Vanholder et al., 2015). Furthermore, the older age at first calving, breed, longer calving interval and dry period, greater 305-day milk yield and lower milk fat yield in the previous lactation, and season acted as risk factors for ketosis in North American dairy herds (Tatone et al., 2017; Mellado et al., 2018). In addition, high BCS, male calves, long calving interval, big herd size (>150 cows), high lactation number, dystocia, metritis, and retained placenta increased susceptibilities to ketosis in South American dairy industry (Garro et al., 2014; Garzón-Audor & Oliver-Espinosa, 2019). Some characteristics, such as lactation number, the age at calving, pregnancy wastage, and retained placenta remain poorly described. There are no reports on certain characteristics, such as the method of reproduction, parturition time, and calf birth weight.

We hypothesized that additional characteristics may be associated with the incidence of ketosis. Thus, we aimed to identify the associations between ketosis and the method of reproduction, parturition time, and calf birth weight. Moreover, we intended to clarify characteristics such as lactation number, the age at calving, pregnancy wastage, and retained placenta, in other studies and to determine the incidence of ketosis during the transition period. Our findings could help predict ketosis, lead to the development of improved management and animal care strategies, and minimize economic loss.

2 | MATERIALS AND METHODS

2.1 | Animals

The cows, used in this study, were raised and calved at a farm in Cheonan, the Republic of Korea. The farm housed approximately 360 cows and calves (Holstein and Jersey) and produced approximately 3000 kg milk daily from nearly 90 dairy cows. The multiparous cows entered the dry period 2 months before due date. Vitamin D was administered to all cows twice, once at 6 weeks and once at 3 weeks before the estimated calving date to prevent milk fever. A total of 186 Holstein cows were used in this study. The cows calved from January 2018 to December 2021 and were milked twice a day in the morning and evening. Dairy cows that were milked less than twice a day or had mastitis, agalactia, theileriosis, milk fever, acidosis, abomasal ulcer, culling, and medication use were excluded. Dairy cows receiving nutritional or microbial supplement capsules and boluses after calving were excluded even though these cows were milked twice a day. In addition, we only included Holstein cows that calved Holstein calves. The lactating animals were fed total mixed rations ad libitum, which consisted of concentrates, soybean meal, corn silage, alfalfa hay, timothy hay, enzyme, minerals, and vitamin additives (dry matter, 63.27 ± 1.78%; crude protein, 15.03 ± 0.92% of dry matter; ether extract, 4.31 ± 0.44% of dry matter; neutral detergent fibre, 37.00 ± 4.80 % of dry matter; acid detergent fibre, 20.79 ± 2.78% of dry matter).

2.2 | β-Hydroxybutyrate test and study design

We performed β-hydroxybutyrate (BHBA) tests once every 3 days (eight times for 21 days from the calving date) during the post-partum transition period. Blood was collected from the jugular vein 6–23 h post-partum and seven times from day three post-partum immediately after the morning milking when cows were fed for analyses of BHBA. BHBA concentrations were determined using an electronic handheld meter (FreeStyle Optimum Neo, Abbott Diabetes Care Ltd., Witney, UK) and β-ketone test strips (FreeStyle Optimum β-Ketone, Abbott Diabetes Care Ltd.) immediately following blood sampling. The cows were divided into three classifications according to the highest BHBA concentration observed from any of the eight post-partum samples as follows: non-ketosis (NK, <1.2 mmol/L, $n = 94$), subclinical ketosis (SCK, ≥1.2 mmol/L and <3.0 mmol/L, $n = 58$), and clinical ketosis (CK, ≥3.0 mmol/L, $n = 34$) (Jeong et al., 2017; Mellado et al., 2018).

2.3 | Data collection

We collected data related to the dairy cows and their calves. Data collected included methods of reproduction (artificial insemination and

embryo transfer), parturition time (day, 06:00–18:00; night, 18:00–06:00), calving season (spring, March to May, 5.2–18.7°C, 64.8%; summer, June to August, 19.7–29.1°C, 77.7%; autumn, September to November, 7.9–19.4°C, 77%; winter December to February, −6.1 to 5.4°C, 65.8%), pregnancy wastage (abortion, calving a calf dead more than 10 days before estimated due date during dry-off period; stillbirth, calving a calf dead less than 10 days before or after estimated due date), premature delivery (calving a live calf more than 10 days before estimated due date), retained placenta (failure to expel placenta within 24 h after parturition), lactation number, BCS at parturition (five-point scale body condition scoring system), age, the calving interval of multiparous cows, types of calves (sex and twins), and Holstein calf birth weight. Holstein calf birth weight was categorized as underweight (<36 kg), normal weight (≥36 kg and ≤45 kg), or overweight (>45 kg), based on the average weight addressed by Holstein Association USA, Inc. Cases of abortion, premature birth, and twins were excluded from the analysis of association between calf birth weight and the severity of ketosis. Daily milk yield was recorded beginning on day four post-partum using an electronic milk meter (Alpro System, DeLaval, Tumba, Sweden) owing to the production of colostrum. Daily milk yield denoted the average of values for the previous three days.

2.4 | Statistical analyses

Statistical analyses were performed using SPSS software (SPSS 26.0, IBM-SPSS INC, Chicago, IL, USA). The linear-by-linear association with two-tailed tests were used to determine the associations between the severity of ketosis and the method of reproduction, parturition time, calving season, pregnancy wastage, premature delivery, retained placenta, previous calving experience, types of calves, and calf birth weight. BCS, age, lactation number, calving interval, daily milk yield, and the daily milk yield from days four to six by the type and calf birth weight data were subjected to analysis of variance with Tukey's honestly significant differences by the severity of ketosis. A linear mixed model with Bonferroni post hoc analysis and repeated-measure analysis of variance were performed to evaluate repeated measurements of the daily milk yield. The time and severity of ketosis were the fixed effects, whereas cows nested within the classification were the random effect. All data are expressed as the mean ± standard error of the means (SEM). Results with p-values <0.05 were considered significant.

3 | RESULTS

3.1 | Association between ketosis and the characteristics of dams

The NK classification represented 50.5% (n = 94) of the population, whereas 31.2% (n = 58) and 18.3% (n = 34) of the population were in the SCK and CK classifications, respectively. The severity of ketosis was not associated with method of reproduction, parturition time, pregnancy wastage, retained placenta, and previous calving experience. The incidence of ketosis in the herd was higher from spring to summer (65.7%) than that from autumn to winter (38.9%) ($p < 0.01$). In terms of the total of SCK and CK, the highest incidence of ketosis occurred in summer (73.7%), followed by spring (57.1%), winter (40.4%), and autumn (37.5%). The incidence of SCK in spring was approximately 16% units lower than that in summer, whereas the incidence of CK was similar between spring and summer (Table 1).

Cows with CK had increased BCS, age, lactation number, and calving interval at parturition ($p < 0.05$) (Table 2). Previous calving experience was not associated with ketosis, whereas the lactation number was associated with the severity of ketosis among multiparous cows ($p < 0.05$). The CK and NK classifications demonstrated the highest and the lowest lactation number, respectively ($p < 0.05$). The severity of ketosis and BCS and age at parturition showed stronger statistical associations in multiparous cows than in primiparous cows. (Tables 1 and 2).

3.2 | Association between ketosis and the characteristics of calves

The severity of ketosis of the dam and calf characteristics are presented in Table 3. The incidence of ketosis was not associated with twins and the sex of the calf. Less dams with twins had ketosis compared with those that had a single calf, but only seven cows had twins in the trial which did not provide sufficient data to adequately evaluate the severity of ketosis. No differences were observed in the severity of ketosis due to the sex of the calf. The calf birth weight was associated with the severity of ketosis ($p < 0.01$). The incidence of ketosis (total of SCK and CK) was higher for cows having calves weighing more than 45 kg (58.1%) compared to those with calves below 36 kg (26.9%) at birth. A higher percentage of dams with an overweight calf (27.9%) suffered from clinical ketosis than those with a normal weight calf (19.6%) (Table 3).

3.3 | Association between ketosis and daily milk yield

The severity of ketosis was associated with the daily milk yield from days four to six ($p < 0.001$). From days four to six, the CK classification produced more milk than the SCK classification, which in turn produced more milk than the NK classification ($p < 0.05$). The daily milk yield of the ketosis classifications fluctuated during the transition period. At the late transition period, the daily milk yield of the CK classification was considerably lower than the other classifications in multiparous cows (Figure 1).

The sex of calves was not associated with the daily milk yield of their dam from day four to six. However, calf birth weight was associated with the daily milk yield of their dam from day four to six. From days four to six, both primiparous and multiparous dams with an underweight calf produced the least milk, whereas those with an overweight calf produced the most milk (Figure 2).

TABLE 1 The severity of ketosis according to variables associated with reproduction

Variable	Level	Number of cows (percentage)			*p*-Value
		NK	SCK	CK	
Total		94 (50.5)	58 (31.2)	34 (18.3)	
Incidence of ketosis by monitoring day	Day 0				
	Day 3		4	2	
	Day 6		15	6	
	Day 9		9	10	
	Day 12		8	6	
	Day 15		4	5	
	Day 18		10	5	
	Day 21		8		
Method of reproduction	Artificial insemination	81 (51.3)	49 (31.0)	28 (17.7)	0.587
	Embryo transfer	13 (46.4)	9 (32.1)	6 (21.4)	
Parturition time	Day (06:00–18:00)	51 (51.0)	31 (31.0)	18 (18.0)	0.887
	Night (18:00–06:00)	43 (50.0)	27 (31.4)	16 (18.6)	
Calving season	Spring	15 (42.9)	11 (31.4)	9 (25.7)	0.006
	Summer	10 (26.3)	18 (47.4)	10 (26.3)	
	Autumn	35 (62.5)	13 (23.2)	8 (14.3)	
	Winter	34 (59.6)	16 (28.1)	7 (12.3)	
	Spring + summer	25 (34.2)	29 (39.7)	19 (26.0)	0.001
	Autumn + winter	69 (61.1)	29 (25.7)	15 (13.3)	
Pregnancy wastage	No	89 (51.1)	55 (31.6)	30 (17.2)	0.264
	Yes	5 (41.7)	3 (25.0)	4 (33.3)	
Premature delivery	No	82 (50.3)	51 (31.3)	30 (18.4)	0.178
	Yes	7 (63.6)	4 (36.4)	0 (0)	
Retained placenta	No	87 (50.6)	54 (31.4)	31 (18.0)	0.852
	Yes	7 (50.0)	4 (28.6)	3 (21.4)	
Previous calving experience	Primiparous	35 (58.3)	14 (23.3)	11 (18.3)	0.342
	Multiparous	59 (46.8)	44 (34.9)	23 (18.3)	

Note: The total of each level was 100% because the total number of each level was different. Pregnancy wastage comprises abortion and stillbirth.
Abbreviations: CK, clinical ketosis classification; NK, non-ketosis classification; SCK, subclinical ketosis classification.

TABLE 2 Body condition score (BCS), age, and lactation number at parturition, and calving interval by the severity of ketosis

Variable	Reproductive status	NK	SCK	CK	*p*-Value
BCS at parturition		3.02 ± 0.04^{a}	3.13 ± 0.05^{a}	3.32 ± 0.07^{b}	<0.001
	Primiparous	3.14 ± 0.06	3.25 ± 0.13	3.46 ± 0.18	0.119
	Multiparous	2.95 ± 0.04^{a}	3.11 ± 0.05^{ab}	3.27 ± 0.06^{b}	<0.001
Age at parturition, years		4.06 ± 0.16^{a}	4.88 ± 0.25^{a}	5.84 ± 0.44^{b}	<0.001
	Primiparous	2.81 ± 0.14	2.86 ± 0.14	3.21 ± 0.30	0.353
	Multiparous	4.81 ± 0.18^{a}	5.53 ± 0.26^{a}	7.10 ± 0.44^{b}	<0.001
Lactation number at parturition		2.06 ± 0.11^{a}	2.47 ± 0.16^{ab}	2.71 ± 0.28^{b}	0.018
	Multiparous	2.69 ± 0.12^{a}	2.93 ± 0.15^{a}	3.52 ± 0.27^{b}	0.005
Calving interval, days	Multiparous	475.0 ± 15.0^{a}	540.5 ± 24.6^{a}	628.0 ± 31.8^{b}	<0.001

Note: Data are expressed as mean ± standard error of the means. Different letters in the same row indicate significant statistical differences ($p < 0.05$, Tukey's test).
Abbreviations: CK, clinical ketosis classification; NK, non-ketosis classification; SCK, subclinical ketosis classification.

TABLE 3 The severity of ketosis according to variables associated with calves

Variable	Level	Number of cows (percentage)			*p*-Value
		NK	SCK	CK	
Type of calves	Female	41 (46.1)	31 (34.8)	17 (19.1)	
	Male	47 (52.2)	26 (28.9)	17 (18.9)	0.154
	Twins	6 (85.7)	1 (14.3)	0 (0)	
Calf birth weight	Underweight (<36 kg)	19 (73.1)	6 (23.1)	1 (3.8)	
	Normal weight (36–45 kg)	49 (45.8)	37 (34.6)	21 (19.6)	0.007
	Overweight (>45 kg)	18 (41.9)	13 (30.2)	12 (27.9)	

Note: The total of each level was 100% because the total number of each level was different.
Abbreviations: CK, clinical ketosis classification; NK, non-ketosis classification; SCK, subclinical ketosis classification.

4 | DISCUSSION

In the present study, ketosis was significantly associated with the calving season, BCS, age, lactation number, calving interval, calf birth weight, and daily milk yield in the early post-partum transition period. This is the first study to identify the association between ketosis and calf birth weight. In addition, we evaluated the associations between the characteristics, including the method of reproduction and parturition time, and the severity of ketosis.

There was no association between ketosis and the method of reproduction, parturition time, pregnancy wastage, premature delivery, retained placenta, previous calving experience, and the type of calves. To the best of our knowledge, no previous study has reported on the methods of reproduction, parturition time, and premature delivery in ketosis. Pregnancy wastage was not associated with ketosis, consistent with previous studies (McArt et al., 2013; Vanholder et al., 2015). The association between retained placenta and ketosis is uncertain in previous studies (Berge & Vertenten, 2014; Vanholder et al., 2015; Garzón-Audor & Oliver-Espinosa, 2019). No association was observed between ketosis and retained placenta in our study. Previous calving experience was not associated with the incidence of ketosis. In terms of the association between ketosis and the type of calves, insufficient data prevented an assessment of the effect of twins versus single offspring. Moreover, the difference between dams with a female calf versus male calf was not significant. In contrast to previous studies (McArt et al., 2013; Garro et al., 2014), dams with a female calf exhibited a slightly increased incidence of ketosis than those with a male calf in this study, although the difference was not significant. All studies, including the previous and current studies, did not report a statistical difference, thus necessitating further studies to evaluate the association between ketosis and the sex of calves.

The incidence of ketosis was associated with the calving season, despite divided opinion on spring or summer season posing the highest risk (Biswal et al., 2016; Dar et al., 2017; Jeong et al., 2017; Mellado et al., 2018). Considering variations in climate and weather in every country, data from Korean studies are more suitable for comparisons with our data. In this study and a previous one, cows calving in summer revealed the highest incidence of ketosis, followed by spring (Jeong et al., 2017). The previous study demonstrated that high temperature and humidity are supposedly associated with ketosis. Despite partial agreement, it did not explain higher incidence of ketosis in spring than that in autumn and winter. This may be attributed to the adjustment of animals to seasonal change. The temperature increases from spring to summer, whereas it falls from autumn to winter. Animals deposit fat in their subcutaneous and visceral adipose tissues while preparing for the cold weather (Reinecke et al., 1982; Prestrud & Nilssen, 1992; Mader, 2003, Giles et al., 2015). Cows that calve during hot weather have less fat (Senosy & Osawa, 2018). Moreover, insulin resistance is greater in warmer months in horses and humans (Bunout et al., 2003; Sadeghpour et al., 2019). Insulin resistance affects the aetiology of ketosis in the transition period of cows (Youssef et al., 2017) and may cause them to consume and reduce more fat from the body in hot weather. Insulin sensitivity may help cows to deposit more body fat in cold weather. Fatty acids are converted to ketone bodies, and this mechanism may rationalize the higher incidence of ketosis in spring and summer.

Findings regarding the association of ketosis with BCS, age, lactation number, and calving interval were consistent with previous findings. Cows with high BCS at calving have an increased risk of ketosis (Duffield, 2000; Gillund et al., 2001; Shin et al., 2015; Tatone et al., 2017). The incidence of ketosis is associated with lactation number or age at calving (Duffield, 2000; McArt et al., 2012; Suthar et al., 2013; Berge & Vertenten, 2014; Vanholder et al., 2015; Biswal et al., 2016; Dar et al., 2017; Jeong et al., 2017; Tatone et al., 2017; Brunner et al., 2019; Garzón-Audor & Oliver-Espinosa, 2019; Mohammed et al., 2019; Nazeer et al., 2019). In the present study, age was more associated with the severity of ketosis than lactation number. Lactation number usually increases as the age of cows at parturition increases. However, age at parturition is inconsistent with lactation number in cows with reproductive disorders. Considering increased age at first calving and longer calving intervals are related to the odds ratio of ketosis, the age at parturition may outweigh lactation number in terms of its association with ketosis (Tatone et al., 2017). The results of the age of primiparous cows and calving interval in the current study reinforce previous findings.

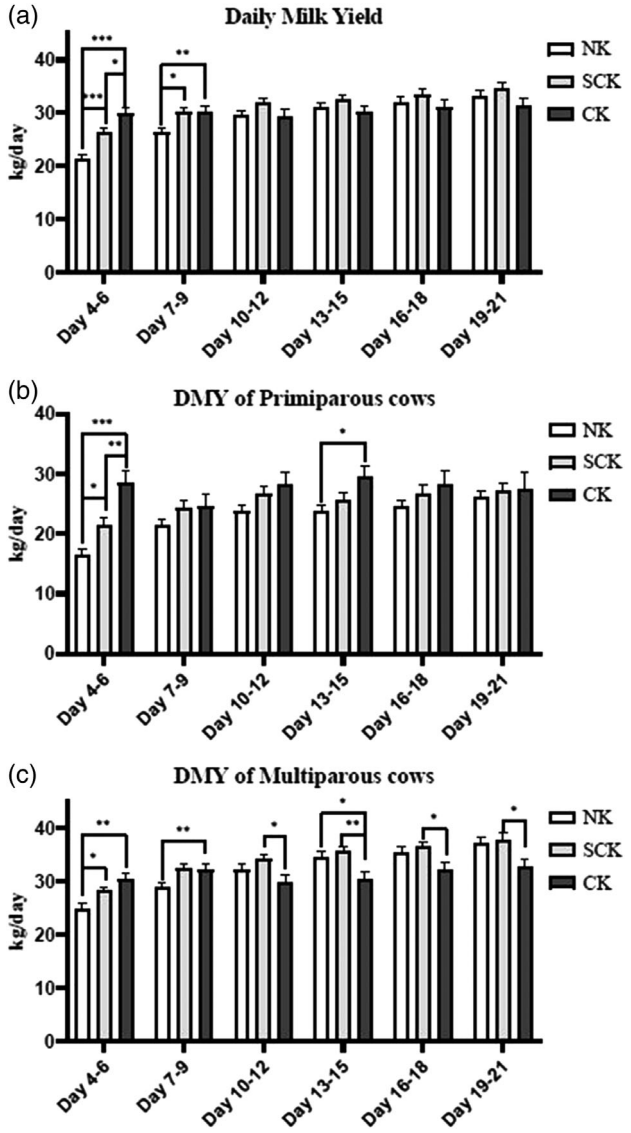

FIGURE 1 Daily milk yield from days 4 to 21 according to the severity of ketosis. (a) Daily milk yield of both primiparous and multiparous cows, (b) daily milk yield of primiparous cows, and (c) daily milk yield of multiparous cows. The means represent the average daily milk yield. Error bars represent the standard error of the means. *p*-Values were determined by Tukey's honestly significant differences. Abbreviations: CK, clinical ketosis classification; DMY, daily milk yield; NK, non-ketosis classification; SCK, subclinical ketosis classification. $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$

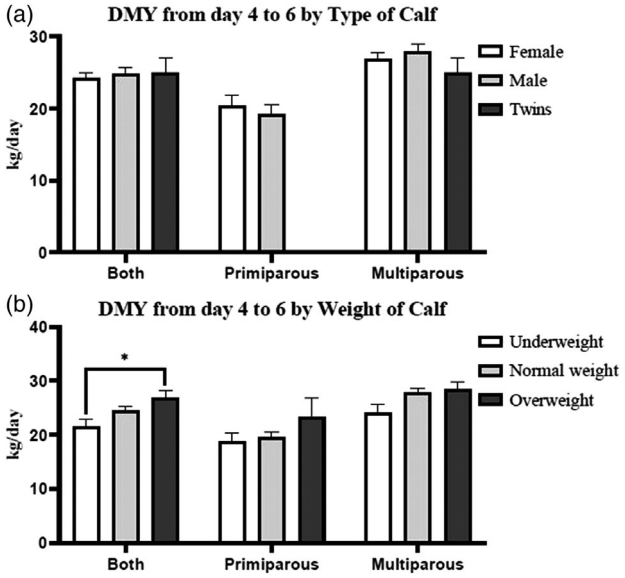

FIGURE 2 Daily milk yield from days 4 to 6 according to the calves. (a) Average daily milk yield from days 4 to 6 by the type of calves and (b) average daily milk yield from days 4 to 6 by the weight of calves. The means represent the average daily milk yield. Error bars represent the standard error of the means. *p*-Values were determined by Tukey's honestly significant differences. Abbreviations: CK, clinical ketosis classification; DMY, daily milk yield; NK, non-ketosis classification; SCK, subclinical ketosis classification. $^{*}p < 0.05$

Negative energy balance occurs in the early lactation period in dairy cows, which can be a condition leading to energy metabolic disorders and result in ketosis. However, the association between ketosis and milk yield was ambiguous in previous studies. Mellado et al. (2018) reported that cows with ketosis had higher 305-day milk yields, whereas Kaufman et al. (2018) reported lower milk yield. These diverging results might originate from the different study designs. The daily milk yield fluctuates during the lactation period, and dairy cows have their own peak milk yield period. This research focused on milk yield at the beginning of the lactation period. In the present study, the severity of ketosis was significantly associated with the daily milk yield in both primiparous and multiparous cows from days four to six. Increased colostrum yield is a risk factor for ketosis (Vanholder et al., 2015). Likewise, increased milk yield during the early transition period may be associated with the severity of ketosis. Further studies are required to investigate the association between ketosis and the peak period of milk production.

Holstein cows that calved a heavier Holstein calf revealed higher incidence and severity of ketosis. We did not find any previous reports on the association between the birth weight of calves and ketosis. The association between calf birth weight and the severity of ketosis may be attributed to the milk yield in the early lactation period. The birth weight of calves was significantly associated with the severity of ketosis and the daily milk yield from day four to six. Cows with a heavier calf always display more lactation performance with earlier peak days (Asaadi et al., 2019). Moreover, early-lactation cows suffer from ketosis (Kaufman et al., 2018). Cows with a heavy calf are likely to develop ketosis during the post-partum transition period.

The limitation of our study was that it was conducted at a single farm. Further research should include more dairy cows from various farms. However, this is the first study to reveal the association between the severity of ketosis and the weight of calves.

5 | CONCULSION

This study investigated the characteristics of Holstein cows predisposed to ketosis during the post-partum transition period. We did not

detect any associations between the severity of ketosis and the method of reproduction, parturition time, pregnancy wastage, premature delivery, retained placenta, and type of calf. The severity of ketosis was significantly associated with the calving season (spring and especially summer), high body condition score at parturition, old age, high lactation number, high daily milk yield in the early transition period, and increased calf birth weight. These findings allow the establishment of preventative strategies for ketosis.

AUTHOR CONTRIBUTIONS

Conceptualization, *data curation*, *formal analysis*, *investigation*, *methodology*, *resources*, *software*, *validation*, *visualization*, *and writing—original draft*: Seungmin Ha. *Investigation and software*: Seogjin Kang. *Investigation and software*: Manhye Han: *Funding acquisition and project administration*: Mooyoung Jeong. *Data curation*: Jihwan Lee. *Formal analysis*: Hakjae Chung. *Conceptualization*, *validation*, *and writing—review and editing*: Jinho Park.

ACKNOWLEDGEMENTS

The authors would like to express their deepest gratitude to Choongkyeong Kim, Sanghun Park, and Youngso Hong for their technical support. This research was funded by "The improvement of animal diseases control in National Institute of Animal Science (Project No. PJ01567603)" project at National Institute of Animal Science, Rural Development Administration, Republic of Korea.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The dataset analyzed in the current study is available from the authors upon reasonable request.

ETHICS STATEMENT

This research was approved by the Institutional Animal Care and Use Committee (IACUC) at the National Institute of Animal Science, the Republic of Korea (approved number: NIAS-2020127). All experimental procedures involving animals were conducted in strict accordance with relevant guidelines and regulations.

ORCID

Seungmin Ha https://orcid.org/0000-0002-5152-1979

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1002/vms3.1006.

REFFERENCES

Asaadi, A., Shiebani, F., & Atashi, H. (2019). Calf birth weight and its association with dam's subsequent lactation performance and lactation curve in Holstein dairy cows in Iran. *Archiva Zootechnica*, *22*(1), 87–101.

Belay, T. K., Svendsen, M., Kowalski, Z. M., & Ådnøy, T. (2017). Genetic parameters of blood β-hydroxybutyrate predicted from milk infrared spectra and clinical ketosis, and their associations with milk production traits in Norwegian Red cows. *Journal of Dairy Science*, *100*(8), 6298–6311.

Benedet, A., Manuelian, C., Zidi, A., Penasa, M., & De Marchi, M. (2019). Invited review: β-hydroxybutyrate concentration in blood and milk and its associations with cow performance. *Animal*, *13*(8), 1676–1689.

Berge, A. C., & Vertenten, G. (2014). A field study to determine the prevalence, dairy herd management systems, and fresh cow clinical conditions associated with ketosis in western European dairy herds. *Journal of Dairy Science*, *97*(4), 2145–2154.

Biswal, S., Nayak, D. C., & Sardar, K. K. (2016). Prevalence of ketosis in dairy cows in milk shed areas of Odisha state, India. *Veterinary world*, *9*(11), 1242.

Brunner, N., Groeger, S., Canelas Raposo, J., Bruckmaier, R. M., & Gross, J. J. (2019). Prevalence of subclinical ketosis and production diseases in dairy cows in Central and South America, Africa, Asia, Australia, New Zealand, and Eastern Europe. *Translational Animal Science*, *3*(1), 84–92.

Bunout, D., Barrera, G., de la Maza, P., Gattas, V., & Hirsch, S. (2003). Seasonal variation in insulin sensitivity in healthy elderly people. *Nutrition*, *19*(4), 310–316.

Cocco, R., Canozzi, M. E. A., & Fischer, V. (2021). Rumination time as an early predictor of metritis and subclinical ketosis in dairy cows at the beginning of lactation: Systematic review-meta-analysis. *Preventive Veterinary Medicine*, *189*, 105309.

Dar, A., Malik, H., Beigh, S., Hussain, S., Nabi, S., Dar, A., Dar, P., & Bhat, A. (2018). Clinico-biochemical alternation in bovine ketosis. *Journal of Entomology and Zoology Studies*, *6*, 1146–1150.

Dar, A., Malik, H., Shah, O., Beigh, S., Hussain, S., Hussain, T., Jan, A., Amin, U., & Nabi, S. (2017). Retrospective and prospective studies on prevalence of Bovine ketosis in Kashmir Valley. *Journal of Entomology and Zoology Studies*, *5*(6), 1832–1835.

Duffield, T. (2000). Subclinical ketosis in lactating dairy cattle. *Veterinary Clinics of North America: Food Animal Practice*, *16*(2), 231–253.

Garro, C. J., Mian, L., & Cobos Roldán, M. (2014). Subclinical ketosis in dairy cows: Prevalence and risk factors in grazing production system. *Journal of Animal Physiology and Animal Nutrition*, *98*(5), 838–844.

Garzón-Audor, A., & Oliver-Espinosa, O. (2019). Incidence and risk factors for ketosis in grazing dairy cattle in the Cundi-Boyacencian Andean plateau, Colombia. *Tropical Animal Health and Production*, *51*(6), 1481–1487.

Giles, S. L., Nicol, C. J., Rands, S. A., & Harris, P. A. (2015). Assessing the seasonal prevalence and risk factors for nuchal crest adiposity in domestic horses and ponies using the Cresty Neck Score. *BMC Veterinary Research*, *11*(1), 1–9.

Gillund, P., Reksen, O., Gröhn, Y., & Karlberg, K. (2001). Body condition related to ketosis and reproductive performance in Norwegian dairy cows. *Journal of Dairy Science*, *84*(6), 1390–1396.

Guliński, P. (2021). Ketone bodies–causes and effects of their increased presence in cows' body fluids: A review. *Veterinary World*, *14*(6), 1492.

Ha, S., Kang, S., Han, M., Lee, J., Chung, H., Oh, S.-I., Kim, S., & Park, J. (2022). Predicting ketosis during the transition period in Holstein Friesian cows using hematological and serum biochemical parameters on the calving date. *Scientific Reports*, *12*(1), 1–9.

Jeong, J.-K., Choi, I.-S., Moon, S.-H., Lee, S.-C., Kang, H.-G., Jung, Y.-H., Park, S.-B., & Kim, I.-H. (2017). Risk factors for ketosis in dairy cows and associations with some blood metabolite concentrations. *Journal of Veterinary Clinics*, *34*(4), 255–260.

Kaufman, E., Asselstine, V., LeBlanc, S., Duffield, T., & DeVries, T. (2018). Association of rumination time and health status with milk yield and composition in early-lactation dairy cows. *Journal of Dairy Science*, *101*(1), 462–471.

LeBlanc, S., Leslie, K., & Duffield, T. (2005). Metabolic predictors of displaced abomasum in dairy cattle. *Journal of Dairy Science*, *88*(1), 159–170.

Lei, M. A. C., & Simões, J. (2021). Invited review: Ketosis diagnosis and monitoring in high-producing dairy cows. *Dairying*, *2*(2), 303–325.

Liang, D., Arnold, L., Stowe, C., Harmon, R., & Bewley, J. (2017). Estimating US dairy clinical disease costs with a stochastic simulation model. *Journal of Dairy Science*, *100*(2), 1472–1486.

Mader, T. L. (2003). Environmental stress in confined beef cattle. *Journal of Animal Science*, *81*(14), E110–E119.

McArt, J., Nydam, D., & Oetzel, G. (2012). Epidemiology of subclinical ketosis in early lactation dairy cattle. *Journal of Dairy Science*, *95*(9), 5056–5066.

McArt, J., Nydam, D., & Oetzel, G. (2013). Dry period and parturient predictors of early lactation hyperketonemia in dairy cattle. *Journal of Dairy Science*, *96*(1), 198–209.

McArt, J., Nydam, D., & Overton, M. (2015). Hyperketonemia in early lactation dairy cattle: A deterministic estimate of component and total cost per case. *Journal of Dairy Science*, *98*(3), 2043–2054.

Mellado, M., Dávila, A., Gaytán, L., Macías-Cruz, U., Avendaño-Reyes, L., & García, E. (2018). Risk factors for clinical ketosis and association with milk production and reproduction variables in dairy cows in a hot environment. *Tropical Animal Health and Production*, *50*(7), 1611–1616.

Mohammed, N., Jaiswal, M., & Bihani, D. K. (2019). Prevalence of subclinical and clinical ketosis in cattle in and around Bikaner. *Biological Rhythm Research*, *53*(4), 1–9.

Mostert, P., Bokkers, E., Van Middelaar, C., Hogeveen, H., & De Boer, I. (2018). Estimating the economic impact of subclinical ketosis in dairy cattle using a dynamic stochastic simulation model. *Animal*, *12*(1), 145–154.

Nazeer, M., Kumar, S., Jaiswal, M., Mishra, A., Upmanyu, G., Kumar, P., & Kumar, S. A. (2019). Prevalence and clinical manifestations of ketosis in cows in and around Bikaner. *International Journal of Current Microbiology and Applied Sciences*, *8*, 1554–1560.

Prestrud, P., & Nilssen, K. (1992). Fat deposition and seasonal variation in body composition of arctic foxes in Svalbard. *The Journal of Wildlife Management*, *56*(2), 221–233.

Raboisson, D., Mounie, M., Khenifar, E., & Maigne, E. (2015). The economic impact of subclinical ketosis at the farm level: Tackling the challenge of over-estimation due to multiple interactions. *Preventive Veterinary Medicine*, *122*(4), 417–425.

Rasmussent, L., Nielsen, B., Pryce, J., Mottram, T., & Veerkamp, R. (1999). Risk factors associated with the incidence of ketosis in dairy cows. *Animal Science*, *68*(3), 379–386.

Reinecke, K. J., Stone, T. L., & Owen Jr, R. B. (1982). Seasonal carcass composition and energy balance of female black ducks in Maine. *The Condor*, *84*(4), 420–426.

Sadeghpour, A., Chalmeh, A., Pourjafar, M., Rezakhani, A., & Badiei, K. (2019). Insulin resistance and its relevance with age, sex, season and obesity in Darehshori horse breed. *Iranian Journal of Veterinary Medicine*, *13*(3), 270–278.

Satoła, A., & Bauer, E. A. (2021). Predicting subclinical ketosis in dairy cows using machine learning techniques. *Animals*, *11*(7), 2131.

Senosy, W., & Osawa, T. (2018). Association among calving season and measures of energy status, resumption of ovulation and subclinical endometritis in early lactating dairy cows. *Animal Reproduction (AR)*, *10*(1), 24–31.

Shin, E.-K., Jeong, J.-K., Choi, I.-S., Kang, H.-G., Hur, T.-Y., Jung, Y.-H., & Kim, I.-H. (2015). Relationships among ketosis, serum metabolites, body condition, and reproductive outcomes in dairy cows. *Theriogenology*, *84*(2), 252–260.

Steeneveld, W., Amuta, P., van Soest, F. J., Jorritsma, R., & Hogeveen, H. (2020). Estimating the combined costs of clinical and subclinical ketosis in dairy cows. *PLoS One*, *15*(4), e0230448.

Sun, Y., Wang, B., Shu, S., Zhang, H., Xu, C., Wu, L., & Xia, C. (2015). Critical thresholds of liver function parameters for ketosis prediction in dairy cows using receiver operating characteristic (ROC) analysis. *Veterinary Quarterly*, *35*(3), 159–164.

Suthar, V., Canelas-Raposo, J., Deniz, A., & Heuwieser, W. (2013). Prevalence of subclinical ketosis and relationships with post-partum diseases in European dairy cows. *Journal of Dairy Science*, *96*(5), 2925–2938.

Tatone, E. H., Duffield, T. F., LeBlanc, S. J., DeVries, T. J., & Gordon, J. L. (2017). Investigating the within-herd prevalence and risk factors for ketosis in dairy cattle in Ontario as diagnosed by the test-day concentration of β-hydroxybutyrate in milk. *Journal of Dairy Science*, *100*(2), 1308–1318.

Vanholder, T., Papen, J., Bemers, R., Vertenten, G., & Berge, A. (2015). Risk factors for subclinical and clinical ketosis and association with production parameters in dairy cows in the Netherlands. *Journal of Dairy Science*, *98*(2), 880–888.

Walsh, R., Walton, J., Kelton, D., LeBlanc, S., Leslie, K., & Duffield, T. (2007). The effect of subclinical ketosis in early lactation on reproductive performance of post-partum dairy cows. *Journal of Dairy Science*, *90*(6), 2788–2796.

Youssef, M. A., El-Ashker, M. R., & Younis, M. S. (2017). The effect of subclinical ketosis on indices of insulin sensitivity and selected metabolic variables in transition dairy cattle. *Comparative Clinical Pathology*, *26*(2), 329–334.

How to cite this article: Ha, S., Kang, S., Jeong, M., Han, M., Lee, J., Chung, H., & Park, J. (2023). Characteristics of Holstein cows predisposed to ketosis during the post-partum transition period. *Veterinary Medicine and Science*, *9*, 307–314. https://doi.org/10.1002/vms3.1006