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Previous Lactation Risk Factors Associated with Hyperketonemia in the First Week Postpartum in Dairy Cows: A Retrospective Analysis

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Abstract: Hyperketonemia (HYK) is a common disorder in high-producing dairy cows, resulting in significant economic losses. Defined by elevated beta-hydroxybutyrate (BHB; ≥1.2 mmol/L) without clinical signs, HYK is often considered a gateway disease, predisposing cows to other metabolic and infectious problems. Our objective was to investigate the association between previous lactation risk factors and both BHB concentration and HYK status during the first week postpartum in the subsequent lactation. A retrospective study was conducted using previously collected blood samples from 2336 Holstein multiparous dairy cows from 7 dairy herds, where BHB concentration was measured during the first week postpartum. Data from the previous lactation were extracted from electronic farm records. Log-transformed BHB concentrations and HYK status were each modeled using separate linear mixed models. Both models included the same set of risk factors—lactation, previous lactation total times bred, dry length period, previous lactation days in milk, previous lactation days open, previous lactation days carried calf, previous lactation peak milk production, previous lactation total milk production, previous lactation total milk fat, and previous lactation total milk protein—to investigate their association with these outcomes. Potential confounding variables were offered to the models, and stepwise backward elimination was used to determine which covariates to retain. Significant associations were detected between BHB concentration and dry period length (DDRY), lactation number (LACT), previous lactation total milk protein (TOTP), and previous lactation days open (PDOPN). Inclusive, significant associations were detected between HYK status and previous lactation total milk production (PTOTM), DDRY, LACT, TOTP, and PDOPN. Our results suggest that a dry period longer than 60 days, days open exceeding 130 days, being in their third or greater lactation, and each additional 1000 kg of milk produced in the previous lactation are associated with an increased risk of having high BHB and HYK in the first week postpartum in the subsequent lactation.

Keywords: dairy cows; herd management; health monitoring; ketosis; transition period

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1. Introduction

Dairy cows experience a nutrient deficit around parturition due to reduced dry matter intake and increased demands for fetal growth, colostrum, and milk production [1,2]. To compensate, they mobilize body reserves, primarily adipose tissue, resulting in the production of ketone bodies that serve as an alternative energy source [3]. Although these adaptations are expected in high-producing cows, excessive mobilization can lead

to elevated circulating fatty acids and ketone bodies, impairing production and immune response [4–6]. Hyperketonemia (HYK), a prevalent finding in high-producing dairy cows during the first two weeks of lactation, is defined by elevated beta-hydroxybutyrate (BHB $\geq$ 1.2 mmol/L) without clinical signs [3,7,8]. It develops because of the unmet energy demands during early lactation, leading to severe negative energy balance [9,10]. Consequently, HYK increases the risk of postpartum disorders, such as displaced abomasum, metritis, and fatty liver, resulting in significant milk losses, increased culling due to poor milk production and reproductive performance, and economic impacts [11–14]. Hyperketonemia is a metabolic disorder closely associated with milk production. Negative nutrient balance, the underlying issue behind HYK, is negatively correlated with milk yield, suggesting that cows that produce more milk are at a greater risk of developing HYK. This relationship has been described by a previous study [15]. Moreover, Oikonomou et al. (2008) [16] reported a relatively high heritability of blood β-hydroxybutyrate (BHB) concentrations during early lactation, reinforcing the notion of a genetic component to HYK. Consequently, ongoing genetic selection for higher milk yield may inadvertently increase the prevalence of HYK in dairy herds.

Several risk factors have been identified in previous studies that may help predict the development of postpartum HYK. Among them, dry period management has been described as a key contributor; effective practices during this time have been associated with a lower risk of HYK [17,18]. In addition, cow-level factors—particularly excessive body condition and inadequate nutrition during the dry period—have consistently emerged as major contributors to HYK risk [19,20]. Other relevant risk factors include prior health issues, parity, calving season, and herd size [19,21,22]. Furthermore, differences in regional and national management strategies can significantly influence the incidence of HYK [21]. Together, these factors provide important insight for predicting HYK and guiding the development of targeted preventive strategies.

Improving our understanding of risk factors associated with postpartum disorders can enhance management and treatment strategies by enabling more targeted allocation of labor and care to cows at greater risk. Therefore, the objective of this study was to retrospectively analyze previously recorded lactation data from herd management software to identify factors associated with elevated blood BHB concentrations and the occurrence of HYK during the first week postpartum in the subsequent lactation. We hypothesized that postpartum BHB concentrations and HYK incidence within the first week of lactation are associated with production parameters and management practices from the preceding lactation.

2. Materials and Methods

A retrospective study was carried out using data collected from 7 commercial dairy farms in Minnesota and Wisconsin in the United States between June 2018 and January 2022. Descriptive information for the seven commercial herds included in the study is presented in Table 1. Data from a total of 2336 multiparous Holstein dairy cows were used in this study. The data used in this analysis were generated in previous studies on hyperketonemia prevalence and the development of predictive algorithms during the first two weeks postpartum. As the samples had already been collected, no additional ethical approval was required. All cows in this study were housed in free-stall barns and were fed non-limiting amounts of prepartum or postpartum total mixed ration according to National Research Council recommendations [23]. Feed was delivered once daily, and cows were milked three times daily.

Table 1. Herd-level descriptive data from the seven commercial dairy farms included in the study.

Item	Herd A	Herd B	Herd C	Herd D	Herd E	Herd F	Herd G
Herd size (n)	690	1526	1287	2071	1368	3445	4417
Lactation, n (%)							
Lactation = 1	255 (37)	560 (37)	447 (35)	800 (39)	452 (33)	1104 (32)	1700 (38)
Lactation = 2	203 (29)	457(30)	394 (30)	536 (26)	379 (28)	1073 (31)	1338 (30)
Lactation $\geq$ 3	232 (34)	509 (33)	446 (35)	735 (35)	537 (39	1268 (37)	1379 (32)
305 d milk yield (kg)	14,276	11,184	13,021	12,560	12,610	12,667	13,036

In the original studies, farms were visited once per week, and blood samples were collected from all multiparous cows in their first week of lactation (1 to 7 days in milk [DIM]). Sampling was conducted in the morning, immediately after cows returned from the milking parlor and fresh feed was delivered. Samples were taken from the coccygeal vessels using a 20-gauge, 2.54 cm blood collection needle and evacuated tubes containing lithium heparin as an anti-coagulant (Vacutainer, Becton Dickinson, Franklin Lakes, USA). Upon collection, blood BHB was measured immediately using a previously validated handheld device (Precision Xtra, Abbott Inc., Bedford, USA; [24]). In accordance with Duffield (2000) [7] and McArt et al. (2012) [8], cows with BHB $\geq$ 1.2 mmol/L were classified as having hyperketonemia (HYK+), while cows with BHB < 1.2 mmol/L were considered to not have hyperketonemia (HYK−). Cow-level data related to the previous lactation risk factors of interest were extracted from each farm's herd management software (Dairy Comp 305, Valley Agricultural Software) to assess their potential association with HYK development during the first week of lactation in the subsequent lactation.

Statistical Analysis

Statistical analyses were conducted using R 4.2.2 (https://www.r-project.org/, accessed on 11 June 2025). Two separate mixed models were executed, one for each outcome. The first was a linear mixed model assessing the association between risk factors and log-transformed BHB concentration in the first week postpartum to address non-normality. The second model is a generalized linear mixed model (GLMM) with a binomial distribution and logit link, evaluating the association between the previous lactation risk factors of interest and the HYK status, categorized as HYK+ or HYK−, in the first week postpartum.

The categorical variable lactation number (LACT) was categorized as lactation = 2 (referent), lactation = 3, and lactation > 3. Additionally, previous lactation total breeding times (PTBRD) were evaluated with PTBRD = 1 as the reference group, compared to categories of 2–4 and more than 4 times. Among the continuous variables, previous lactation total milk production (PTOTM) was analyzed per 1000 kg increment and previous lactation total milk protein (PTOTP) per 100 kg increment. To improve interpretability and address multicollinearity, the variable PTOTM was mean centered before inclusion in the model. The centered variable (PTOTM_c) was obtained by subtracting the mean of PTOTM from each individual value. Additionally, instead of using the raw squared term ($PTOTM^2$), we included the squared form of the centered variable ($PTOTM_c^2$) to better capture potential nonlinear relationships while maintaining orthogonality between linear and quadratic terms. This approach was necessary, as the Variance Inflation Factor (VIF) was high when including both PTOTM and $PTOTM^2$ in the model, indicating multicollinearity.

In contrast, the remaining continuous variables did not meet the assumption of linearity, based on Shapiro–Wilk test results, and were categorized for both univariable and multivariable analyses. Dry period length (DDRY) was categorized as <30 days, 30 to 60 days (referent), and >60 days. Previous lactation days in milk (PDIM) were categorized as

<285 days, 285 to 305 days (referent), and >305 days. Previous lactation days open (PDOPN) was divided into <100 days, 100 to 130 days (referent), 130 to 160 days, and >160 days. Previous days carried calf (PDCC), or gestation length, was divided into <260 days, 260 to 280 days (referent), and >280 days. Previous lactation peak milk production (PPEAK) was divided as <40 kg (referent), 40 to 50 kg, 50 to 60 kg and >60 kg. Lastly, previous lactation total milk fat (PTOTF) was categorized as <300 kg (referent), 300 to 700 kg, and >700 kg. All identified risk factors were initially evaluated using univariable models for both outcomes of interest, with only those variables yielding a p-value < 0.2 retained for subsequent multivariable analyses. Retained variables were then examined for collinearity using the Spearman rank correlation coefficient, with a threshold of $\geq$0.7 indicating collinearity. The final linear mixed model for each outcome was built by manual stepwise backward elimination, with variables retained when $p < 0.05$. Confounders were assessed and kept in the models only if their removal changed the coefficients of the remaining variables by >20%. The effect of herd was forced as a random effect in all models. Possible interactions were checked and retained in the models when $p < 0.05$. To improve the interpretability of the linear mixed model results, which used log-transformed BHB as the outcome, the estimated coefficients were exponentiated and reported as percentage changes in BHB concentration. Visual inspection with quartile normal plots was used to determine whether the residuals followed a normal distribution. In addition to this, standardized residuals were graphically plotted against predicted outcomes to look for influential observations that had a significant impact on the model.

3. Results

3.1. Descriptive Results

The average blood BHB concentration across all cows included in the study was 0.89 ± 0.65 mmol/L. When categorized by HYK status, mean BHB concentrations were 0.67 mmol/L for HYK− cows and 1.91 mmol/L for HYK+ cows. The average 305-day projected total milk yield (PTOTM) and projected total milk protein yield (PTOTP) were 12,800 ± 3200 kg (range: 2295 to 30,627 kg) and 412 ± 104 kg (range: 85 to 979 kg), respectively (Table 2). Among enrolled cows, 965 were entering their second lactation, 696 their third, and 675 were in their fourth or greater lactation (Table 3). The distribution of cows by lactation number and other previous lactation risk factors evaluated in this study is detailed in Table 3.

Table 2. Mean values of blood beta-hydroxybutyrate (BHB), previous total milk production (PTOTM), and previous lactation total milk protein (PTOTP) in the study herds.

Variable *	Herd A (N = 53)	Herd B (N = 599)	Herd C (N = 131)	Herd D (N = 191)	Herd E (N = 252)	Herd F (N = 410)	Herd G (N = 700)	Overall (N = 2336)
BHB (mmol/L)	0.87 (0.61)	0.67 (0.32)	1.10 (1.09)	0.73 (0.36)	0.94 (0.78)	0.95 (0.66)	1.04 (0.70)	0.89 (0.65)
PTOTM (kg)	13,000 (2330)	11,700 (2490)	13,200 (2880)	9770 (2250)	12,800 (2460)	13,000 (2680)	14,500 (3760)	12,800 (3200)
PTOTP (kg)	401 (68)	380 (81)	425 (82)	308 (65)	401 (78)	409 (79)	472 (119)	412 (104)

* Values presented as mean (standard deviation).

Table 3. The total number of cows (percentage) through qualitative variables and descriptive of quantitative variables recorded for 2336 dairy cows from 7 dairy herds.

Variable	Herd A (N = 53)	Herd B (N = 599)	Herd C (N = 131)	Herd D (N = 191)	Herd E (N = 252)	Herd F (N = 410)	Herd G (N = 700)	Overall (N = 2336)
Hyperketonemia								
HYK−	46 (86.8%)	562 (93.8%)	93 (71.0%)	175 (91.6%)	206 (81.7%)	323 (78.8%)	508 (72.6%)	1913 (81.9%)
HYK+	7 (13.2%)	37 (6.2%)	36 (27.5%)	16 (8.4%)	46 (18.3%)	87 (21.2%)	192 (27.4%)	421 (18.0%)
Missing	0 (0%)	0 (0%)	2 (1.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.1%)

Table 3. *Cont.*

Variable	Herd A (N = 53)	Herd B (N = 599)	Herd C (N = 131)	Herd D (N = 191)	Herd E (N = 252)	Herd F (N = 410)	Herd G (N = 700)	Overall (N = 2336)
Lactation								
2	22 (41.5%)	225 (37.6%)	54 (41.2%)	76 (39.8%)	105 (41.7%)	172 (42.0%)	311 (44.4%)	965 (41.3%)
3	15 (28.3%)	185 (30.9%)	34 (26.0%)	65 (34.0%)	80 (31.7%)	113 (27.5%)	204 (29.2%)	696 (29.8%)
>3	16 (30.2%)	189 (31.5%)	43 (32.8%)	50 (26.2%)	67 (26.6%)	125 (30.5%)	185 (26.4%)	675 (28.9%)
Previous lactation times bred								
1	46 (86.8%)	315 (52.6%)	90 (68.7%)	67 (35.1%)	157 (62.3%)	174 (42.4%)	232 (33.2%)	1081 (46.3%)
(2–4)	7 (13.2%)	263 (43.9%)	37 (28.2%)	122 (63.9%)	86 (34.1%)	218 (53.2%)	381 (54.4%)	1114 (47.7%)
>4	0 (0%)	21 (3.5%)	4 (3.1%)	2 (1.0%)	9 (3.6%)	18 (4.4%)	87 (12.4%)	141 (6.0%)
Peak milk production in previous lactation								
<40 kg	1 (1.9%)	154 (25.7%)	8 (6.1%)	56 (29.3%)	61 (24.2%)	90 (22.0%)	85 (12.1%)	455 (19.5%)
>40–50 kg	9 (17.0%)	230 (38.4%)	29 (22.1%)	57 (29.8%)	105 (41.7%)	118 (28.8%)	182 (26.0%)	730 (31.2%)
>50–60 kg	16 (30.2%)	177 (29.6%)	38 (29.0%)	58 (30.4%)	63 (25.0%)	134 (32.7%)	228 (32.6%)	714 (30.6%)
>60 kg	27 (50.9%)	38 (6.3%)	56 (42.7%)	20 (10.5%)	23 (9.1%)	68 (16.5%)	205 (29.3%)	437 (18.7%)
Previous lactation days in milk								
<285 days	0 (0%)	41 (6.8%)	1 (0.8%)	22 (11.5%)	4 (1.6%)	1 (0.2%)	39 (5.6%)	108 (4.6%)
285–305 days	46 (86.8%)	180 (30.1%)	83 (63.4%)	67 (35.1%)	139 (55.1%)	106 (25.9%)	145 (20.7%)	766 (32.8%)
>305 days	7 (13.2%)	378 (63.1%)	47 (35.8%)	102 (53.4%)	109 (43.3%)	303 (73.9%)	516 (73.7%)	1462 (62.6%)
Days dry								
<30 days	1 (1.8%)	9 (1.5%)	0 (0%)	0 (0%)	2 (0.8%)	0 (0%)	7 (1.0%)	19 (0.8%)
30–60 days	49 (92.5%)	455 (76.0%)	115 (87.8%)	165 (86.4%)	228 (90.5%)	322 (78.5%)	375 (53.6%)	1709 (73.2%)
>60 days	3 (5.7%)	135 (22.5%)	16 (12.2%)	26 (13.6%)	22 (8.7%)	88 (21.5%)	318 (45.4%)	608 (26.0%)
Previous lactation days carrying calf								
<260 days	1 (1.9%)	10 (1.7%)	1 (0.8%)	0 (0%)	1 (0.4%)	2 (0.5%)	13 (1.9%)	28 (1.2%)
260–280 days	50 (94.3%)	303 (50.6%)	94 (71.8%)	144 (75.4%)	162 (64.3%)	193 (47.1%)	375 (53.6%)	1321 (56.6%)
>280 days	2 (3.8%)	286 (47.7%)	36 (27.4%)	47 (24.6%)	89 (35.3%)	210 (51.2%)	312 (44.5%)	982 (42.0%)
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (1.2%)	0 (0%)	5 (0.2%)
Previous lactation days open								
<100 days	49 (92.5%)	385 (64.3%)	99 (75.6%)	131 (68.6%)	179 (71.0%)	201 (49.0%)	220 (31.4%)	1264 (54.1%)
>100–130 days	4 (7.5%)	106 (17.7%)	13 (9.9%)	43 (22.5%)	38 (15.1%)	94 (22.9%)	130 (18.6%)	428 (18.3%)
>130–160 days	0 (0%)	55 (9.2%)	12 (9.2%)	15 (7.9%)	16 (6.4%)	61 (14.9%)	146 (20.9%)	305 (13.1%)
>160 days	0 (0%)	53 (8.8%)	7 (5.3%)	2 (1.0%)	19 (7.5%)	50 (12.2%)	204 (29.1%)	335 (14.3%)
Missing	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (1.0%)	0 (0%)	4 (0.2%)
Previous lactation total fat								
<300 kg	0 (0%)	22 (3.7%)	5 (3.8%)	67 (35.1%)	3 (1.2%)	2 (0.5%)	15 (2.1%)	114 (4.9%)
300–700 kg	53 (100%)	569 (95.0%)	123 (93.9%)	124 (64.9%)	233 (92.5%)	390 (95.1%)	567 (81.0%)	2059 (88.1%)
>700 kg	0 (0%)	8 (1.3%)	3 (2.3%)	0 (0%)	16 (6.3%)	18 (4.4%)	118 (16.9%)	163 (7.0%)

HYK: hyperketonemia "HYK+ = BHB $\geq$ 1.2 mmol/L, HYK− = BHB < 1.2 mmol/L".

3.2. Multivariable Linear Mixed Model and BHB

The relationship between previous lactation milk production and BHB concentration was nonlinear, as indicated by the significant quadratic term (PTOTM_c^2, $p = 0.006$). The linear term (PTOTM_c) was not significant ($p = 0.53$), suggesting that the overall trend is best captured by a U-shaped curve. Based on the model estimates, BHB concentration tends to increase with milk production at both lower and higher levels, indicating a potential U-shaped association. Specifically, for every 1000 kg increase in milk production, BHB concentration is expected to increase by approximately 1.1%.

There was a significant association between DDRY and BHB concentration, with BHB concentration for DDRY < 30 days being 25.2% lower ($p = 0.008$) than the referent group (DDRY between 30 and 60 days). Based on model estimates, and assuming all other variables are held at their reference levels, the predicted BHB concentration for cows with DDRY between 30 and 60 days was approximately 0.96 mmol/L, corresponding to a reduction to about 0.72 mmol/L in cows with a dry period of <30 days. Conversely, BHB concentration for cows with DDRY > 60 days was 9.4% higher (BHB concentration 1.05 mmol/L, $p < 0.001$) than the referent group (Figure 1). There was a significant associa-

tion between lactation number and BHB concentration ($p < 0.001$). Compared to second lactation, BHB concentrations were 23.4% and 32.3% higher in cows in their third lactation and lactation > 3, respectively (Figure 1). There were no significant associations between PTBRD 2–4 ($p = 0.29$) and PTBRD more than 4 ($p = 0.07$) and BHB concentrations (Table 3, Figure 1). Moreover, there was no evidence of an association between PDIM < 285 days and PDIM > 305 days and BHB concentration in the first week of the subsequent lactation ($p = 0.26$ and 0.24, respectively) (Figure 1). Previous lactation total protein was associated ($p = 0.002$) with BHB concentration in the first week of the subsequent lactation. The BHB concentration in the next lactation was 11.3 kg lower for each 100 kg increase in PTOTP. There was no significant difference in BHB concentrations for cows with PDOPN less than 100 days compared to the referent group (PDOPN 100–130 days; $p = 0.65$). Conversely, BHB concentrations for cows with PDOPN between 130 and 160 days and >160 days were 11.6% ($p = 0.003$) and 28.4% ($p < 0.001$) higher than the referent group, respectively (Figure 1).

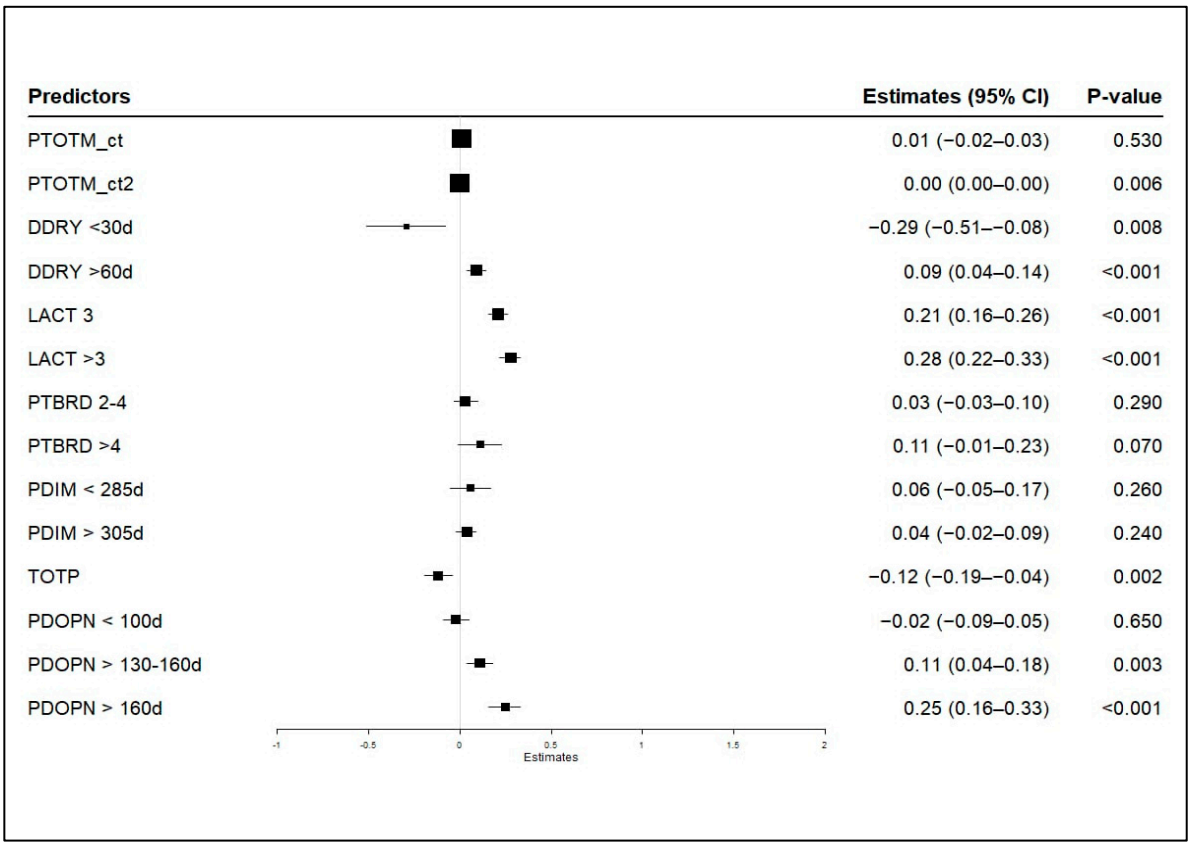


Figure 1. Forest plot for effect of different risk factors on log beta-hydroxybutyrate (BHB) in 2336 dairy cows. PTOTM_ct: centered previous total milk production; PTOTM_ct2: centered and squared previous total milk production; DDRY: dry period days; LACT: lactation; PTBRD: previous total breeding; PDIM: previous days in milk; TOTP: total milk protein; PDOPN: previous days open; *p* value significant at the level of <0.05.

3.3. Generalized Linear Mixed Model and HYK Status

There was a significant association ($p = 0.01$) between PTOTM and the incidence of HYK in the first week of the subsequent lactation. The odds ratio for HYK was 1.19 (95% CI: 1.05, 1.35) higher for every 1000 kg increase in PTOTM. There was no significant difference ($p = 0.52$) in the odds of HYK for cows with a DDRY of less than 30 days compared to cows with a dry period length between 30 and 60 days (OR: 0.60; 95% CI: 0.13, 2.84). However, the risk of HYK increased with longer dry periods, as cows with DDRY greater than 60 days had 1.69 times higher odds of HYK (95% CI: 1.30, 2.20) compared to the referent group. The

odds ratios for HYK in the third lactation and in lactations ≥ 4 were 2.64 (95% CI: 1.95, 3.58) and 3.90 (95% CI: 2.85, 5.34), respectively, compared to the second lactation ($p < 0.001$). No evidence of an association was observed between PTBRD 2–4 (OR: 0.97; 95% CI: 0.66, 1.42; $p = 0.87$) and PTBRD more than 4 (OR: 1.15; 95% CI: 0.62, 2.14; $p = 0.65$) and risk for HYK (Figure 2). Previous lactation total milk protein produced was associated ($p < 0.001$) with HYK status in the next lactation, with the odds ratio for HYK being 0.44 (95% CI: 0.29, 0.67) lower for each 100 kg increase in TOTP. Compared to the referent group (PDOPN 100–130), the odds of HYK were not significantly different for cows with PDOPN less than 100 days (OR: 0.71; 95% CI: 0.47, 1.08; $p = 0.11$), but were significantly higher for cows with PDOPN 130–160 days (OR: 1.52; 95% CI: 1.02, 2.26; $p = 0.04$) and PDOPN greater than 160 days (OR: 3.02; 95% CI: 1.95, 4.67; $p < 0.001$) (Figure 2).

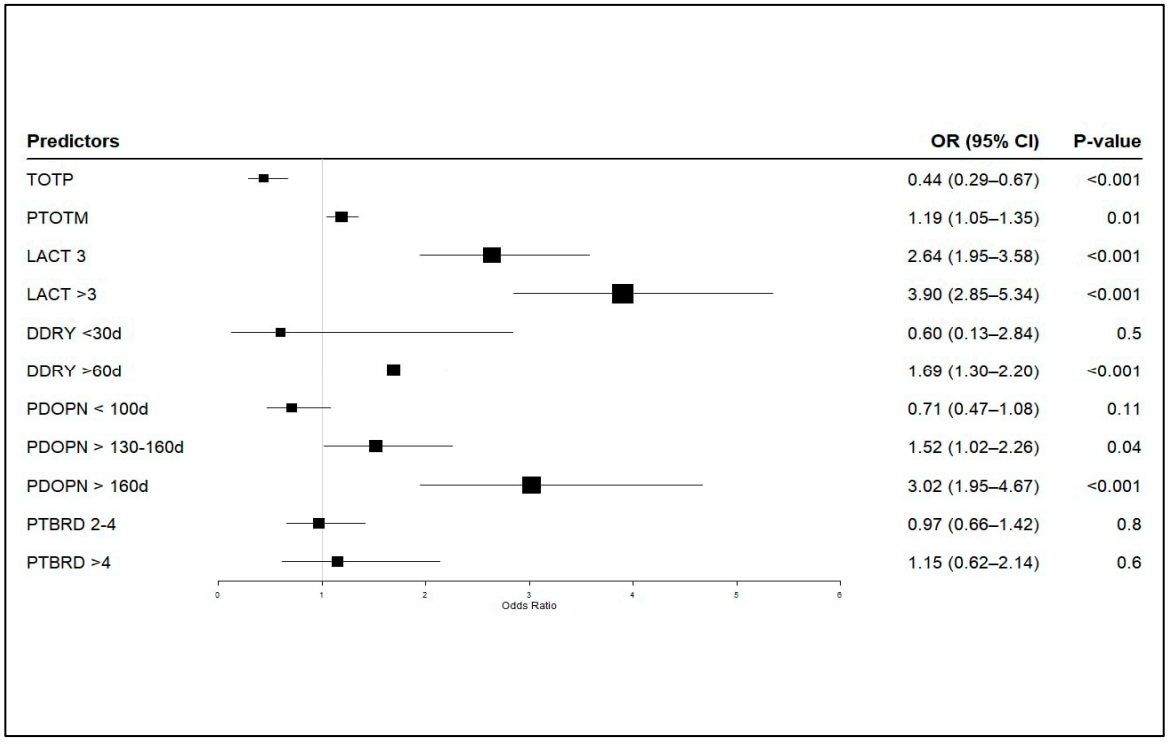


Figure 2. Forest plot for effect of different risk factors on hyperketonemia in 2336 dairy cows. Cows with BHB ≥ 1.2 mmol/L are classified as positive for hyperketonemia (HYK+). Otherwise, it is considered negative with BHB < 1.2 mmol/L (HYK−). TOTP: total milk protein; PTOTM: previous total milk production; LACT: lactation; DDRY: dry period days; PDOPN: previous days open; PTBRD: previous total breeding. The *p*-value is significant at the level of <0.05.

4. Discussion

The current exploratory study aimed to investigate associations between previous lactation risk factors—recorded through farm management software—and both blood BHB concentration and the occurrence of HYK during the first week postpartum in the subsequent lactation. While previous studies have explored the link between earlier lactation data and HYK or BHB concentration, our study expanded on this by analyzing cows from multiple herds to generate more generalizable information, thereby enhancing dairy practitioners' understanding of HYK epidemiology. Significant associations were detected between BHB concentration and DDRY, LACT, PTOTP, and PDOPN. Inclusive, significant associations were detected between HYK status and PTOTM, DDRY, LACT, TOTP, and PDOPN.

Shortening the dry period has been proposed to mitigate the reduction in feed intake before calving and improve energy balance around parturition [25,26] as well as improve

the milk production in the subsequent lactation [27]. In our study, dry periods longer than 60 days were associated with higher BHB concentration and postpartum HYK, while no evidence of an association was observed for shorter dry period length (less than 30 days). Fat mobilization might be one of the reasons for our findings, as previous research suggests that cows with longer dry periods are more likely to gain excess body condition, calve with a higher body condition score, and subsequently mobilize more during the periparturient period [28]. This increased lipid mobilization consequently increased their risk of developing HYK postpartum. Consistent with our findings, previous studies have reported that cows with a shortened dry period had lower postpartum plasma concentrations of NEFA and BHB compared to those with a more traditional dry period length [28,29]. Pezeshki and colleagues [27] similarly found that reducing the dry period to 35 days in primiparous cows decreased serum NEFA concentrations during the periparturient period; however, these cows also produced less milk than those with a 56-day dry period. In contrast, Rastani and colleagues [30] reported no differences in plasma NEFA, BHB, or glucose concentrations between cows within the recommended dry period length (30 to 60 days). Their findings further support our results, suggesting that maintaining an appropriate dry period length reduces the risk of postpartum HYK, whereas an excessively long dry period may increase susceptibility to this disorder.

However, despite the lack of association between shorter dry periods and BHB concentration or HYK occurrence, it remains essential to consider an appropriate dry period length to support overall lactation performance and udder health. A review of previous research has indicated that a dry period of at least 30 days is necessary to optimize milk yield and mammary gland recovery in the subsequent lactation [31]. Therefore, our findings on the lack of association between short dry period length and BHB concentrations or HYK postpartum should be carefully interpreted within a broader management context rather than in isolation.

This study described a significant association between lactation number and both BHB concentration and HYK postpartum, with greater parity having an increased risk for high BHB and HYK. These findings align with previous research indicating that advanced parity is a major risk factor for HYK [14,21,22,28]. Moreover, higher parity cows have been reported to exhibit greater BHB concentration during the first 2 weeks postpartum compared to primiparous cows [9,32]. Older cows generally produce more milk than younger cows, placing greater metabolic demands on them during early lactation. As a result, these cows might rely more heavily on the mobilization of body reserves. This increased dependence on body reserves, including lipid mobilization, leads to higher circulating concentrations of NEFA and BHB compared to younger cows [33,34].

In our study, the risk of postpartum HYK in the first week of the subsequent lactation was significantly associated with PTOTM level. In agreement with our results, a previous study found previous lactation milk production to be a potential risk factor for postpartum HYK in the subsequent lactation [20]. However, Gordon [35] reported no association between PTOTM and risk for postpartum HYK. Another study mentioned that dairy cows with high PTOTM suffer from the high concentration of milk BHB in the subsequent lactation [36]. This study differed from our work by using milk BHB measurement as an indicator of HYK, which is not the industry standard for diagnosis of HYK. In our study, the association between PTOTM and HYK was slightly attenuated after adjusting for LACT, suggesting potential confounding. Higher milk production is often associated with older cows, who may exhibit different metabolic adaptations and disease risks. Since LACT represents parity, the observed relationship between PTOTM and HYK may, in part, reflect differences in the parity of the cows. Extended lactation lengths can lead to excessive body condition score (BCS) at the start of the dry period, mostly due to the positive energy

balance that typically occurs in late lactation [20]. In this study, no significant association was detected between PDIM and either BHB concentration or HYK. Similarly, Vanholder et al. (2015) [21] reported no association between longer PDIM and the risk of HYK. Other studies, however, identified PDIM as a strong predictor of clinical ketosis postpartum [19] and elevated BHB concentration in milk [36].

These findings support the need for proactive identification and monitoring of high-producing cows, especially those in later parities, as they are more likely to develop HYK. Management strategies could include enhanced metabolic screening in early lactation or tailored nutritional interventions during the dry period and early postpartum period. Future research should investigate whether targeted monitoring and intervention strategies in this high-risk group can reduce HYK incidence and improve overall health and productivity.

The PDOPN was significantly associated with both increased BHB concentrations and a greater likelihood of postpartum HYK, with longer days open increasing the risk for each of these outcomes. Extended days open and multiple breeding attempts can lead to an increased body condition score at dry-off and the subsequent calving, reducing dry matter intake during the periparturient period. This, in turn, increased fat mobilization, exacerbated negative energy balance postpartum, and ultimately increased the likelihood of HYK [37,38]. Days open, defined as the interval between parturition and subsequent conception, is an indicator of reproductive success in dairy herds [39]. Prolonged days open not only delay conception but also reduce overall herd profitability, as shorter intervals between calvings enable cows to spend more of their productive life in peak lactation, resulting in greater lifetime milk yield and more calves [40,41]. Several factors influence the duration of the postpartum conception period, including body condition score during the transition period, parity, milk yield, and peripartum disorders [42–44]. While these factors have been well studied, limited research has explored the relationship between days open and HYK in subsequent lactations. The findings from this study help fill this gap by demonstrating that cows with prolonged days open are more likely to experience elevated BHB concentrations postpartum.

The comparison of herd-level data highlights notable differences in metabolic health and production outcomes across a range of herd sizes. For example, Herd A—contributing the fewest cows to our dataset (N = 53)—exhibited relatively low BHB concentrations alongside favorable production metrics, suggesting that this herd achieved a strong performance under effective management. Similarly, Herd F appeared to maintain a balance between milk yield and metabolic stability. In contrast, herds contributing more cows, such as Herd G, while achieving higher milk production, presented with elevated BHB levels, possibly reflecting greater metabolic strain associated with high-yielding systems.

While these observations offer valuable insights, direct comparisons between herds should be interpreted with caution. Herd size often correlates with differences in management style, labor intensity, and consistency of care, all of which can influence metabolic outcomes. Smaller herds may benefit from more individualized attention, whereas larger operations often face greater logistical complexity. These findings suggest that favorable outcomes are achievable across herd sizes, but further research is needed to clarify the role of specific management practices in driving these results.

Another limitation of our study is the absence of body condition score (BCS) data, which could have provided additional context regarding cow health and energy status. However, our objective was to assess associations based solely on data routinely recorded in farm management software, without the need for cow-side measurements. As such, BCS fell outside the scope of this analysis. Future studies should consider incorporating BCS and similar cow-level assessments to deepen understanding of the links between metabolic indicators and performance.

A further limitation lies in the lack of detailed documentation on the specific management strategies used across the seven participating farms, each of which likely operated under different conditions. These differences could influence outcomes and decision-making in ways that are difficult to quantify. To mitigate the potential confounding effects of farm-level variation, herd was included as a random intercept in all models, allowing for the adjustment of unmeasured, farm-specific factors and improving the robustness of our estimates.

Building on the discussion of herd-level variability and study design considerations, another important methodological aspect is the timing of blood sampling. The wide range of blood sampling days reflects our intentional decision to sample cows once per week, in alignment with common farm management practices at the time when the blood sampling was carried out. As a result, cows were at different stages within their first week of lactation (i.e., different DIM) at the time of sampling. This approach allowed us to include a larger number of animals and capture a realistic representation of early lactation, including cows sampled before 3 DIM—a time point often underrepresented in the existing literature due to the tendency to avoid early postpartum sampling.

5. Conclusions

The current study revealed that a dry period of more than 60 days in length, previous lactation days open for more than 130 days, and being in their third or greater lactation are potential risk factors for cows that will have high BHB and HYK in the first week postpartum in the subsequent lactation. Moreover, each additional 1000 kg of milk produced in the previous lactation is associated with an increased risk of postpartum HYK. Identifying key risk factors for HYK in dairy cattle improves our ability to detect and predict cows that are more likely to have this disorder postpartum, allowing more effective management and treatment strategies. Our findings suggest that high-producing, older cows should be considered at increased risk for HYK and may benefit from closer monitoring and tailored management during the transition period. Future research should evaluate whether implementing such targeted strategies, alongside cow-level assessments such as body condition scoring, can improve early detection and prevention of metabolic disorders in dairy herds.

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