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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

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ABSTRACT

The aim of this study was to estimate genetic parameters for blood β-hydroxybutyrate (BHB) predicted from milk spectra and for clinical ketosis (KET), and to examine genetic association of blood BHB with KET and milk production traits (milk, fat, protein, and lactose yields, and milk fat, protein, and lactose contents). Data on milk traits, KET, and milk spectra were obtained from the Norwegian Dairy Herd Recording System with legal permission from TINE SA (Ås, Norway), the Norwegian Dairy Association that manages the central database. Data recorded up to 120 d after calving were considered. Blood BHB was predicted from milk spectra using a calibration model developed based on milk spectra and blood BHB measured in Polish dairy cows. The predicted blood BHB was grouped based on days in milk into 4 groups and each group was considered as a trait. The milk components for test-day milk samples were obtained by Fourier transform mid-infrared spectrometer with previously developed calibration equations from Foss (Hillerød, Denmark). Veterinarian-recorded KET data within 15 d before calving to 120 d after calving were used. Data were analyzed using univariate or bivariate linear animal models. Heritability estimates for predicted blood BHB at different stages of lactation were moderate, ranging from 0.250 to 0.365. Heritability estimate for KET from univariate analysis was 0.078, and the corresponding average estimate from bivariate analysis with BHB or milk production traits was 0.002. Genetic correlations between BHB traits were higher for adjacent lactation intervals and decreased as intervals were further apart. Predicted blood BHB at first test day was moderately genetically correlated with KET (0.469) and milk traits (ranged from −0.367 with protein content to 0.277 with milk yield), except for milk fat content from across lactation stages that had near zero genetic correlation with BHB (0.033). These genetic correlations indicate that a lower BHB is genetically associated with higher milk protein and lactose contents, but with lower yields of milk, fat, protein, and lactose, and with lower frequency of KET. Estimates of genetic correlation of KET with milk production traits were from −0.333 (with protein content) to 0.178 (with milk yield). Blood BHB can routinely be predicted from milk spectra analyzed from test-day milk samples, and thereby provides a practical alternative for selecting cows with lower susceptibility to ketosis, even though the correlations are moderate.
Key words: β-hydroxybutyrate, clinical ketosis, milk trait, genetic parameter

INTRODUCTION

Clinical ketosis (**KET**) is one of the most frequent metabolic diseases affecting dairy cattle. In a recent literature review, Pryce et al. (2016) found a median ketosis frequency of 3.3% with a range from 0.24% in first lactation up to 17.2% in third lactation. Those authors reported a median incident rate of 10.25% for Norwegian Red (**NRF**) cows based on 2 previous studies. The frequency of KET in NRF cows has decreased markedly since the mid-1980s, from 10.6% in 1987 to 4.3% in 1998 in first-lactation cows (Heringstad et al., 2005) and from 23.88% in 1985 to 4.56% in 2005 (Østerås et al., 2007).

In Norway, health data including KET have been recorded on an individual cow basis since 1978 based on veterinarian treatments (Heringstad et al., 2000). Many metabolic events, including ketosis, are subclinical by nature, and information on subclinical cases is mostly missing in records because it is difficult to detect (Pryce et al., 2016). Subclinical cases are assumed to receive less veterinary intervention, thus leading to underestimation of the incidence in systems that depend on veterinary data (Schwarzenbacher et al., 2010). Failure

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to detect subclinical events can be expensive to dairy producers, as it negatively affects overall performance of cows (Duffield et al., 2009); therefore, systems to detect ketosis at a subclinical stage in addition to the clinical one would be useful.

Previous genetic studies of ketosis were mostly based on clinical records. Heritability estimates for KET reported in those studies ranged from 0.01 to 0.16, as summarized in the literature review by Pryce et al. (2016). Heritability estimates for KET may be influenced by the subjective nature of its diagnosis and the low frequency of KET compared with subclinical ketosis in cows (van der Drift et al., 2012b). Moreover, response to selection in KET is hampered by low reliabilities often associated with the low heritability (Pryce et al., 2016). Pryce et al. (2016) suggested that information from correlated traits or from subclinical diagnosis could be used to improve the accuracy of predicted breeding values and increase the selection response. Phenotypes derived from routinely collected data through milk recording, such as fat-to-protein ratio and fatty acid profiles, are promising ketosis indicators (van Knegsel et al., 2010). Phenotypes more closely associated with ketosis, such as BHB and acetone in milk (Pryce et al., 2016), may also be valuable. Concentration of BHB in blood has been used as a gold standard indicator of ketosis, and thresholds of 1.2 (van der Drift et al., 2012a) or 1.4 mmol/L (Denis-Robichaud et al., 2014) have been used to identify cows with subclinical ketosis. However, the gold standard method does not allow routine testing of all animals at risk due to practical limitations, such as difficulty in blood sampling (especially for farmers) and capacity for analyzing many blood samples at a time.

Routine measurements of ketone bodies in milk can be done by Fourier transform mid-infrared (**FT-MIR**) spectrometer analysis of milk samples at test-days (de Roos et al., 2007; van der Drift et al., 2012a; Grelet et al., 2016). Those previous studies agreed that FT-MIR predicted milk ketone bodies adequately and that FT-MIR might be useful for ketosis-screening purposes. In addition to their routine availability, indicator traits (e.g., milk or blood BHB) have moderate heritability (0.07 to 0.40; Oikonomou et al., 2008; van der Drift et al., 2012b; Jamrozik et al., 2016). Milk BHB has also moderate genetic correlations with KET, with estimates ranging from 0.25 to 0.75 (Koeck et al., 2014, 2016; Jamrozik et al., 2016); hence, indirect selection for ketosis using BHB as an indicator trait should result in better genetic gain than direct selection for KET. For example, Koeck et al. (2016) estimated about 65% more selection response from indirect selection for the indicator trait (BHB) than direct selection for ketosis.

Ketone bodies have not routinely been measured by FT-MIR spectrometer analysis of milk samples at test days in Norway. Given the subclinical nature of ketosis, the potential of FT-MIR for routine prediction of ketosis indicators, and the moderate heritability and genetic correlations of the indicator traits with KET, it is important to assess the potential of FT-MIR predicted phenotypes (e.g., BHB) for their use in dairy farm management and breeding programs. For use and implementation of blood BHB predicted from milk spectra in dairy cattle breeding programs, knowledge of genetic parameters and their genetic associations with clinical events and other traits in the breeding goal is essential. Few reports exist on genetic studies of plasma BHB measured by reference methods (Oikonomou et al., 2008; van der Drift et al., 2012b); however, there is no report on genetic parameters and associations of blood BHB predicted from milk spectra with KET and milk production traits for cows in early lactation. Therefore, the objective of our study were (1) to describe the phenotype of predicted blood BHB and to examine its phenotypic associations with KET and milk production traits; (2) to estimate genetic parameters for the predicted blood BHB traits and KET; and (3) to determine genetic associations between the predicted blood BHB and KET and milk production traits (milk, fat, protein, and lactose yields, and milk fat, protein, and lactose contents) in NRF cows.

MATERIALS AND METHODS

Data and Data Edits

We used 3 data sets, referred to as data set 1, data set 2, and data set 3.

Data Set 1. This data set consisted of test-day predicted blood BHB and milk production traits. Over 5 million FT-MIR spectra from milk test-day samples recorded from February 2007 to June 2014 were obtained from the Norwegian dairy herd recording system. The milk spectra were from test-day milk samples analyzed by FT-MIR spectrometer (Milkoscan Combifoss 6500, Foss Electric, Hillerød, Denmark). Blood BHB was predicted from milk spectra of the NRF cows with a previously developed calibration model for blood BHB from milk spectra and reference blood BHB of Polish dairy cows (Belay et al., 2017) by permission from our Polish collaborators (Polish Federation of Cattle Breeders and Dairy Farmers, Warsaw, Poland). The data set consisted of 826 Polish dairy cows (1 observation per cow), from 5 to 65 DIM, with measured blood BHB and milk spectra. It was randomly divided into a calibration (n = 496) and a validation (n = 330) set. The calibration model was developed by partial least square (**PLS**) regression, internally cross-validated using 10 random segments, and externally validated using the

Table 1. Number of records and summary statistics of data set 1 for blood BHB predicted from milk spectra at 11 to 30 (BHB_1), 31 to 60 (BHB_2), 61 to 90 (BHB_3), and 91 to 120 DIM (BHB_4) and across early lactation stage (11–120 DIM; BHB_{all})

Trait	Period, DIM	No. of records	Mean, mmol/L	SD, mmol/L	Minimum, mmol/L	Maximum, mmol/L
BHB_1	11–30	241,543	1.242	0.337	−1.919	6.133
BHB_2	31–60	350,560	1.209	0.293	−4.047	6.317
BHB_3	61–90	327,462	1.170	0.266	−1.163	6.050
BHB_4	91–120	307,573	1.157	0.256	−3.264	4.211
BHB_{all}	11–120	1,227,138	1.192	0.289	−4.047	6.317

validation set. Optimum number of PLS factors (in this case 6 factors) were determined based on first local minimum value in root mean squared error of prediction. The PLS regression coefficients were applied on the Norwegian milk spectra to predict blood BHB. The predicted blood BHB was merged with milk production traits and other farm and cow information. Milk production traits, such as milk fat, protein, and lactose contents, were also predictions from the same spectra with machine integrated operational calibrations for the respective traits (Foss Analytical A/S, Hillerød, Denmark).

The predicted blood BHB and milk production traits were kept for cows in 11 to 120 DIM. Cows with unknown sires or dams, herds with less than 200 test day records, and sires with less than 25 daughters were excluded from further analysis. Only cows with age at calving of 18 to 40, 30 to 51, 42 to 63, and 52 to 74 mo in the first, second, third, and fourth lactations, respectively, were considered. To get a reasonable number of records for age classes at peripheries in each age category, the first and last few age classes were merged into the next and preceding age class, respectively. Number of records per herd test date (**HTD**) were kept to at least 2. Twelve observations with extreme values (potential outliers) were also removed from the data set. The final edited data set contained 1,227,138 test day records from 324,920 cows that were progeny of 1,427 sires and kept in 3,539 herds. Statistical analyses were carried out for the BHB across lactation number in early lactation at periods of 11 to 30 (**BHB_1**), 31 to 60 (**BHB_2**), 61 to 90 (**BHB_3**), and 91 to 120 DIM (**BHB_4**), and across all periods of early lactation, 11 to 120 DIM (**BHB_{all}**). Descriptive statistics of BHB are presented in Table 1. Summary of descriptive statistics for the milk production traits across the lactation stages considered are shown in Table 2. The BHB was found to be reasonably normally distributed (Figure 1) and not log-transformed for genetic analysis. A pedigree file containing animals with records and their ancestors was also available with a total number of 671,849 individuals.

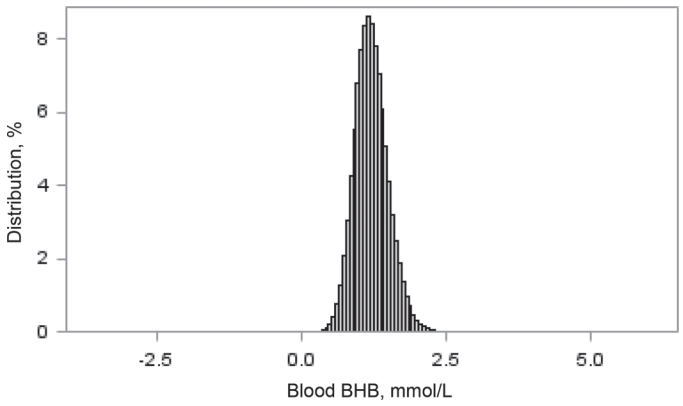

Figure 1. Distribution (%) of blood BHB concentrations (mmol/L) predicted from milk spectra of Norwegian Red cows in data set 1.

Data Set 2. This data set contained information on KET. It consisted of 1,742,421 observations on cows in lactation 1 to 4 that gave birth from January 2007 through December 2015. Absence or presence of KET was scored as 0 or 1, respectively, based on whether or not the cow received veterinary treatment between 15 d before calving to 120 d after calving. For genetic analysis, animals with no sire or dam information and cows with less than 2 records were excluded. The final edited data set consisted of 1,054,381 records from 357,474 cows that were progeny of 2,455 sires and 282,657 dams and kept in 12,533 herds. Statistical analyses were carried out for the KET across lactation numbers. A summary of descriptive statistics of the analyzed data set is presented in Table 2. A pedigree file for animals with records and their ancestors was also available and contained 886,401 individuals.

Data Set 3. The unedited data set of predicted blood BHB and milk production traits was merged with the unedited ketosis data set, keeping only cows with information on BHB. The merged data (data set 3) contained 1,520,446 records from 430,389 cows kept in 11,697 herds. Bivariate genetic analysis of such a large data set was not feasible as the number of elements in mixed model equations were beyond the limit of the program used for REML estimates. Cows with no sire or dam information, small herds (with <225 records

Table 2. Number of records and summary statistics for milk production traits based on data set 1 and for clinical ketosis as binary trait (0 = healthy, 1 = treated) across lactations based on data set 2

Trait	No. of records	Mean	SD	Minimum	Maximum
Milk yield, kg	1,227,138	29.215	6.992	5	50
Fat yield, kg	1,227,138	1.178	0.351	0.094	3.440
Protein yield, kg	1,227,138	0.945	0.219	0.127	2.864
Lactose yield, kg	1,227,138	1.385	0.333	0.090	2.625
Fat, %	1,227,138	4.050	0.789	1.750	7.000
Protein, %	1,227,138	3.250	0.254	1.350	6.980
Lactose, %	1,227,138	4.743	0.180	1.100	5.600
Ketosis, %	1,054,381	2.040	1.414	0	1

over all lactations), and sires with less than 30 daughters were excluded. The final edited merged data set contained 717,915 records from 179,691 cows that were a progeny of 1,169 sires and 135,985 dams and kept in 2,828 herds. The pedigree file of animals with records and their ancestors contained 469,672 individuals.

Models

Data were analyzed with mixed linear animal models using the REML method with parameter expanded and average information algorithm (PX-AI) of the WOMBAT software (Meyer, 2007) or the DMU package (Madsen and Jensen, 2008). Univariate analyses of BHB traits, bivariate analyses among BHB traits, and BHB traits with milk production traits were done using WOMBAT (Meyer, 2007). Bivariate analysis of KET with either BHB or milk production traits were done using the DMU package (Madsen and Jensen, 2008), as DMU allows to fit separate models for each trait in bivariate analyses.

Genetic Parameters for Blood BHB. The test day-predicted blood BHB records were considered as repeated measurement of the same trait across and within lactations. We assumed constant genetic variance across lactation stages and unity genetic correlations between test day records. Hence, predicted blood BHB across stages of early lactation (11–120 DIM) was analyzed with a single-trait repeatability test day animal model. The test day records of BHB were also grouped into adjacent DIM intervals, and each group was treated as a distinct trait and analyzed with single- or multiple-trait repeatability test day animal models. Single- and 2-trait repeatability test day animal models were applied to BHB at 11 to 30, 31 to 60, 61 to 90, and 91 to 120 DIM using the data set 1. In matrix notation, the models were as follows

$$\mathbf{y} = \mathbf{Xb} + \mathbf{Za} + \mathbf{Wc} + \mathbf{Hd} + \mathbf{e}, \qquad [1]$$

where $\mathbf{y}$ is the vector of predicted blood BHB at different DIM intervals or across DIM; $\mathbf{b}$ is a vector of fixed effects of region × year × month of test day, region × parity × DIM, herd × year of test day, parity × age at calving, and housing × milking system; $\mathbf{a}$ is a vector of random animal additive genetic effects; $\mathbf{c}$ is a vector of random permanent environmental (**PE**) effects due to the cow; $\mathbf{d}$ is a vector of random HTD effects; $\mathbf{e}$ is vector of random residual effects; and $\mathbf{X}$, $\mathbf{Z}$, $\mathbf{W}$, and $\mathbf{H}$ are design matrices that relate records to the corresponding effects. Region had 9 levels; DIM was defined in 3 (or 11) classes of 10 d each. Interaction of housing type (tiestall or loose housing) and milking system (robot milking or manual milking: bucket, pipe, and milking parlor) was also modeled. All these fixed effects significantly ($P < 0.001$) affected the traits.

The assumed (co)variance structure in the single-trait analysis was $\text{var}(a) = \sigma_a^2\mathbf{A}$, $\text{var}(p) = \sigma_{pe}^2\mathbf{I}$, $\text{var}(d) = \sigma_d^2\mathbf{I}$, and $\text{var}(e) = \sigma_e^2\mathbf{I}$, where σ_a^2 was additive genetic variance, σ_{pe}^2 was PE variance, σ_d^2 was HTD variance, and σ_e^2 was residual variance. The $\mathbf{I}$ were identity matrices of appropriate sizes and $\mathbf{A}$ was the additive relationship matrix.

For 2-trait analyses, the following covariance structures were assumed for the random effect vectors included in the models:

$$\text{var}\begin{bmatrix}\mathbf{a}\\ \mathbf{c}\\ \mathbf{d}\\ \mathbf{e}\end{bmatrix} = \begin{bmatrix}\mathbf{G}\otimes\mathbf{A} & 0 & 0 & 0\\ 0 & \mathbf{P}\otimes\mathbf{I} & 0 & 0\\ 0 & 0 & \mathbf{J}\otimes\mathbf{I} & 0\\ 0 & 0 & 0 & \mathbf{R}\otimes\mathbf{I}\end{bmatrix},$$

where $\mathbf{G}$ was the genetic covariance matrix, $\mathbf{P}$ was the PE covariance matrix, $\mathbf{J}$ was the covariance matrix for HTD effects, and $\mathbf{R}$ was the residual covariance matrix. All covariance matrices were 2 × 2; $\mathbf{I}$ and $\mathbf{A}$ were as defined above; and ⊗ was the Kronecker product.

Genetic Parameters for KET. A single-trait linear repeatability animal model was applied on data set 2 to estimate genetic parameters for KET. Threshold models are believed to be more appropriate to analyze binary traits, at least in theory. In previous studies on

NRF health data, multivariate threshold models were used (Heringstad et al., 2005); however, mixed linear models were applied in the current study. In their literature review, Pryce et al. (2016) indicated that linear models have performed equally well and are comparable to results from threshold models; several recent studies have also used linear models for ketosis (Koeck et al., 2014, 2016; Jamrozik et al., 2016). Moreover, genetic correlations are reported to be correct for binary traits using linear models (Negussie et al., 2008). In matrix notation, the following linear animal model was applied to the binary ketosis trait:

$$\mathbf{ket} = \mathbf{Xb} + \mathbf{Za} + \mathbf{Wc} + \mathbf{Hy} + \mathbf{e}, \quad [2]$$

where **ket** was a vector of ketosis coded as 0 or 1 (per cow and lactation); **b** was a vector of systematic effects, including region × year× month of calving, parity × age at calving, and housing × milking system; **a** was a vector of random animal additive genetic effects; **c** was a vector of cows' random PE effects; **y** was a vector of random herd-year-month (**HY**) of calving effects; **e** was vector of random residual effects; and **X**, **Z**, **W**, and **H** were design matrices that relate records to the corresponding effects. Classes for age at calving were formed in the same way as for equation [1]. Assumptions of variance structures were also the same as in equation [1] for the single-trait analysis.

Genetic Associations Among BHB, KET, and Milk Production Traits. For bivariate analysis of BHB traits with milk production traits, the same model as in equation [1] was applied using data set 1. Bivariate analyses of BHB traits or milk production traits with KET were done using data set 3. In the bivariate analysis of BHB traits or milk production traits with KET, 2 models were fitted: equation [1] for BHB traits or milk production traits, and equation [2] for KET using the AI-REML procedure in the DMU package (Madsen and Jensen, 2008).

RESULTS AND DISCUSSION

Phenotypic Description of BHB

Concentrations of blood BHB predicted from milk spectra ranged from −4.047 to 6.317 mmol/L, with an average of 1.192 mmol/L and a standard deviation of 0.289 mmol/L (Table 1). This was slightly higher than reference blood BHB values presented by Denis-Robichaud et al. (2014; average of 1.14 mmol/L, with values ranging from 0.2 to 6.3) and Belay et al. (2017), who found an average of 0.760 mmol/L with values ranging from 0.1 to 6.3 for Polish blood sample data. These values were also higher than predicted blood BHB from Polish dairy cows with the same calibration model as that used in the current study (Belay et al., 2017; average of 0.770 mmol/L, with values ranging from 0.492 to 3.95 mmol/L). Higher predicted blood BHB values in the current study than our previous study might have resulted from differences in spectral profile due to management (e.g., feeding), breed, or equipment used to produce spectra (Milkoscan Combifoss 6500 vs. MilkoScan FT6000). Unlike the reference methods, FT-MIR spectroscopy analysis may produce negative values; they account for about 0.004% of the observations in data set 1. These negative values may suggest very low concentrations of BHB in milk. Both the negative and nonnegative predicted blood BHB values were considered in the genetic analysis to be existing variation in the data.

Mean predicted blood BHB concentration at each DIM was calculated and is depicted in Figure 2. Generally, the mean predicted blood BHB concentration was higher in the beginning of lactation and decreased as DIM progressed. This result was in line with previous reports on milk BHB predicted from milk spectra (Koeck et al., 2014) and blood BHB measured with reference method (Belay et al., 2017). Predicted blood BHB decreased up to 20 DIM, and then increased again between 20 and 30 DIM. This is in agreement with a report of Oetzel (2007), who found an increase in predicted blood BHB from 20 to 35 DIM. The rise in BHB between 20 and 30 DIM might be due to ketosis type I that occurs between 3 and 6 wk postcalving, because cows are entering a peak lactation and these cows simply cannot keep up with energy demand mostly because of underfeeding (Oetzel, 2007).

We wanted to determine if models developed for Polish dairy cows could work and give some reasonable results with Norwegian data. We were surprised to find

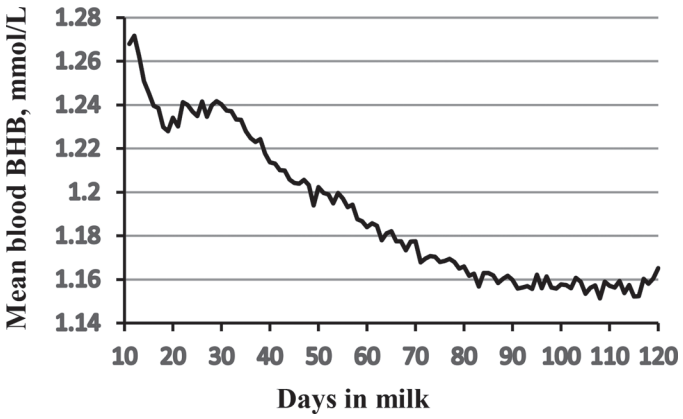

Figure 2. Mean blood BHB (mmol/L) predicted from milk spectra by DIM in first to fourth lactation Norwegian Red cows in data set 1.

that the performance of the models with Norwegian data was reasonable. The phenotypic distribution of the predicted blood BHB, its heritability, and phenotypic and genetic associations with ketosis and milk traits were reasonable and in agreement with most of the published values. More interestingly, at a threshold (≥1.2 mmol/L) that is commonly used to discriminate heathy from ketotic cows, the predicted blood BHB correctly classified more than 77% of the treated cows as ketotic cows. This is a practical validation of the model and does not mean that the models perfectly fitted the Norwegian data. The models might better fit data from the population that was used in the model development. Effects of different breeds and environments would be present, but might not hinder the use of the model in a different breed and environment where a calibration of milk spectra to blood BHB is not available.

Frequency of KET

Mean frequency and standard deviation of veterinary-diagnosed KET across lactations based on data set 2 are given in Table 2. The mean frequency of KET across lactations that was 2.04% in data set 2 was reduced to 1.76% in data set 3, as not all animals diagnosed for KET might have recorded spectra or vice versa. Frequency of KET observed in the current study was lower than in previous studies on NRF cows. Using data from only first-crop daughters of NRF sires that were progeny tested from 1978 through 1998, Heringstad et al. (2005) reported mean frequency of KET ranging from 7.5% in first-lactation to 17.2% in the third-lactation cows.

Phenotypic Associations of BHB with KET and Milk Traits

To investigate phenotypic associations of predicted blood BHB with KET and milk production traits, cows were grouped into 2 categories based on their predicted blood BHB test for risk of ketosis: negative (BHB <1.2 mmol/L), or positive (BHB ≥1.2 mmol/L). The threshold of ≥1.2 mmol/L was used because most authors have used that value (Rollin et al., 2010; van Knegsel et al., 2010; van der Drift et al., 2012a). Figure 3 shows phenotypic associations of cows with positive and negative predicted blood BHB test across early lactation (11–120 DIM) with test-day milk yield, milk fat, protein, and lactose contents, and KET. Mean milk yield for cows with positive predicted blood BHB test increased up to 42 DIM and rapidly decreased afterward, whereas the increase in milk yield lasted up to 60 DIM for cows with negative predicted blood BHB test (<1.2 mmol/L). During the first 2 mo of lactation, mean milk yield from cows with a positive test was higher than for cows with a negative test (Figure 3a). This indicates that high-yielding cows had higher blood BHB concentration and were possibly more prone to the risk of developing ketosis in early lactation compared with lower-yielding cows. The difference in mean milk yield between cows with negative and positive test decreased for DIM up to 68 DIM and almost overlapped afterward.

In addition, cows with a positive predicted blood BHB test had a higher milk fat content throughout the early lactation stage compared with cows with a negative test (Figure 3b). However, cows with a positive predicted blood BHB test had a lower content of milk protein throughout the lactation stages considered compared with cows with a negative test (Figure 3c). Mean milk lactose content for both cows with positive and negative BHB test increased up to 30 DIM and decreased afterward. Cows with positive predicted blood BHB test had lower milk lactose content throughout the lactation stage compared with cows with a negative test (Figure 3d). As expected, cows with positive test for predicted blood BHB had higher frequency of KET (3.41%) compared with cows with negative test (1.01%) (Figure 3e). This indicated that 77.15% of cows with KET were categorized with a positive predicted blood BHB test. Koeck et al. (2014) also observed higher frequency of KET among cows testing positive (≥0.20 mmol/L of milk BHB, 10.8%), followed by cows classified as suspect (≤0.15–0.20 mmol/L of milk BHB, 5.4%) and negative (<0.15 mmol/L of milk BHB, 2.3%).

Phenotypic Associations of KET with BHB and Milk Traits

To study phenotypic associations of KET with predicted blood BHB and milk production traits, cows in data set 3 were grouped as nontreated (healthy) or treated (diseased) based on absence or presence of veterinary treatment for ketosis, respectively. The mean test day predicted blood BHB, milk yield, and milk fat, protein, and lactose contents between 11 and 120 DIM from cows treated by veterinarian for ketosis or not (KET) are given in Figure 4. Mean predicted blood BHB of cows with KET was higher in early lactation, but decreased rapidly with stage of lactation toward the level found in more healthy cows (Figure 4e). Means of predicted blood BHB traits at different DIM intervals were also calculated for cows with and without KET (Table 3). Cows with KET had higher means ($P < 0.05$) for the predicted blood BHB in all lactation stages. The means of predicted blood BHB both at each DIM and at the different DIM intervals

found in the current study were in agreement with the finding of Koeck et al. (2016) in Canadian dairy cows between 5 and 100 DIM.

Cows with KET had slightly higher mean milk yield in early lactation up to around 22 DIM, but slightly lower afterward up to around 60 DIM compared with healthy cows (Figure 4a). This again supported the idea that high-yielding cows are more prone to the risk of KET in early lactation compared with low-yielding cows. Contrary to the current finding, Koeck et al. (2013) reported that cows with KET had a slightly lower milk yield in early lactation compared with healthy cows in first lactation.

In our study, mean milk fat content in both cows with and without KET decreased in early lactation up to 60 DIM. Afterward, the mean milk fat content stabi-

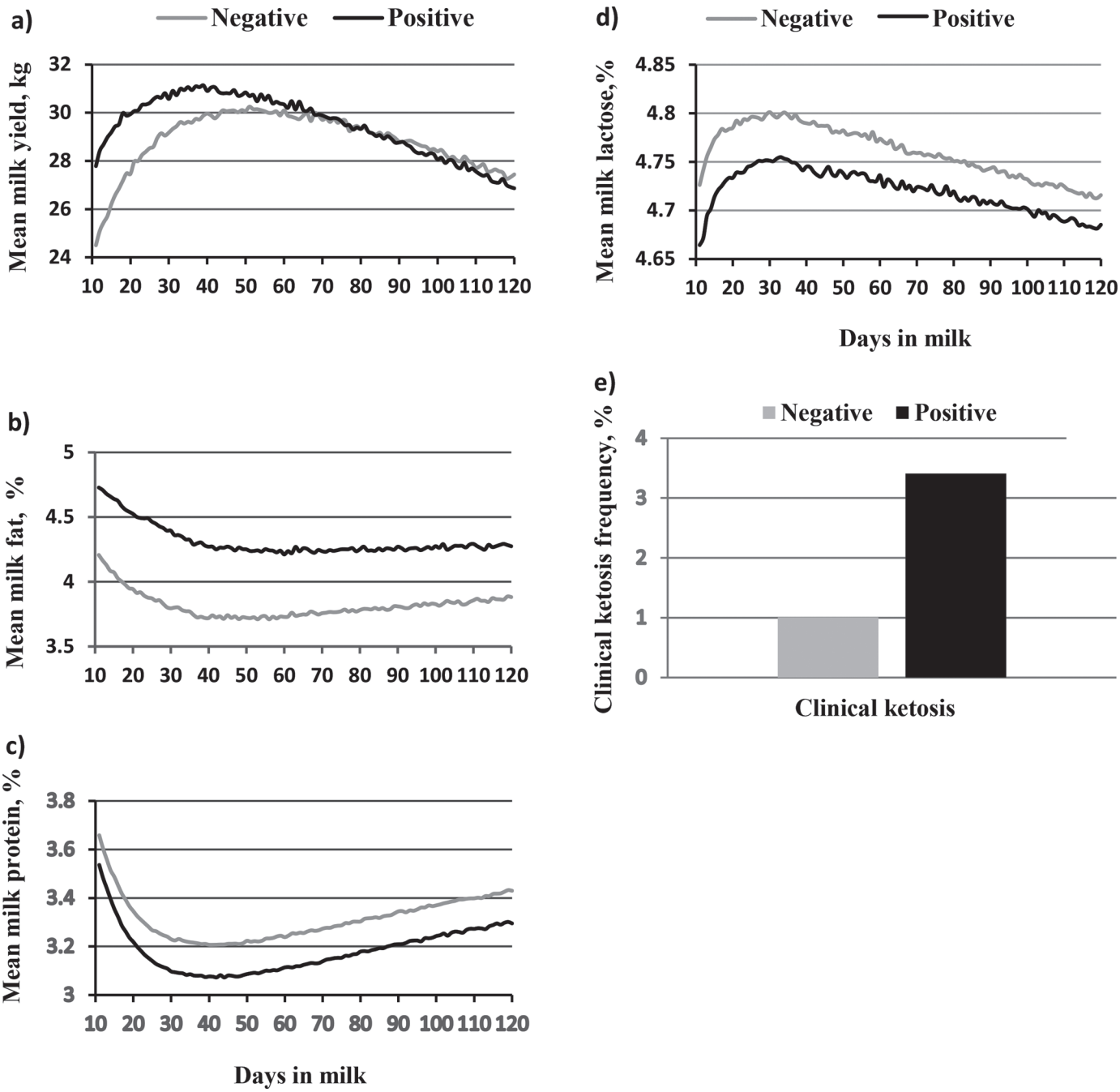

Figure 3. Mean (a) milk yield, (b) milk fat content, (c) protein content, (d) lactose content, and (e) frequency of clinical ketosis by DIM for cows with a negative (BHB <1.2 mmol/L) or positive (BHB ≥1.2 mmol/L) test result for risk of ketosis until 120 d after calving.

lized at an average value of around 4% (Figure 4b). The mean milk fat content from cows with KET was higher in early lactation compared with healthy cows, whereas the mean milk protein content from cows with KET was slightly lower at every DIM compared with healthy cows (Figure 4c). In support of the current finding, Koeck et al. (2013) found higher mean milk fat content but a slightly lower milk protein content in cows with KET compared with healthy cows both at the first (5–30 DIM) and second test day (31–60 DIM). The mean milk lactose content from both cows with and without KET increased to about 30 DIM. Afterward,

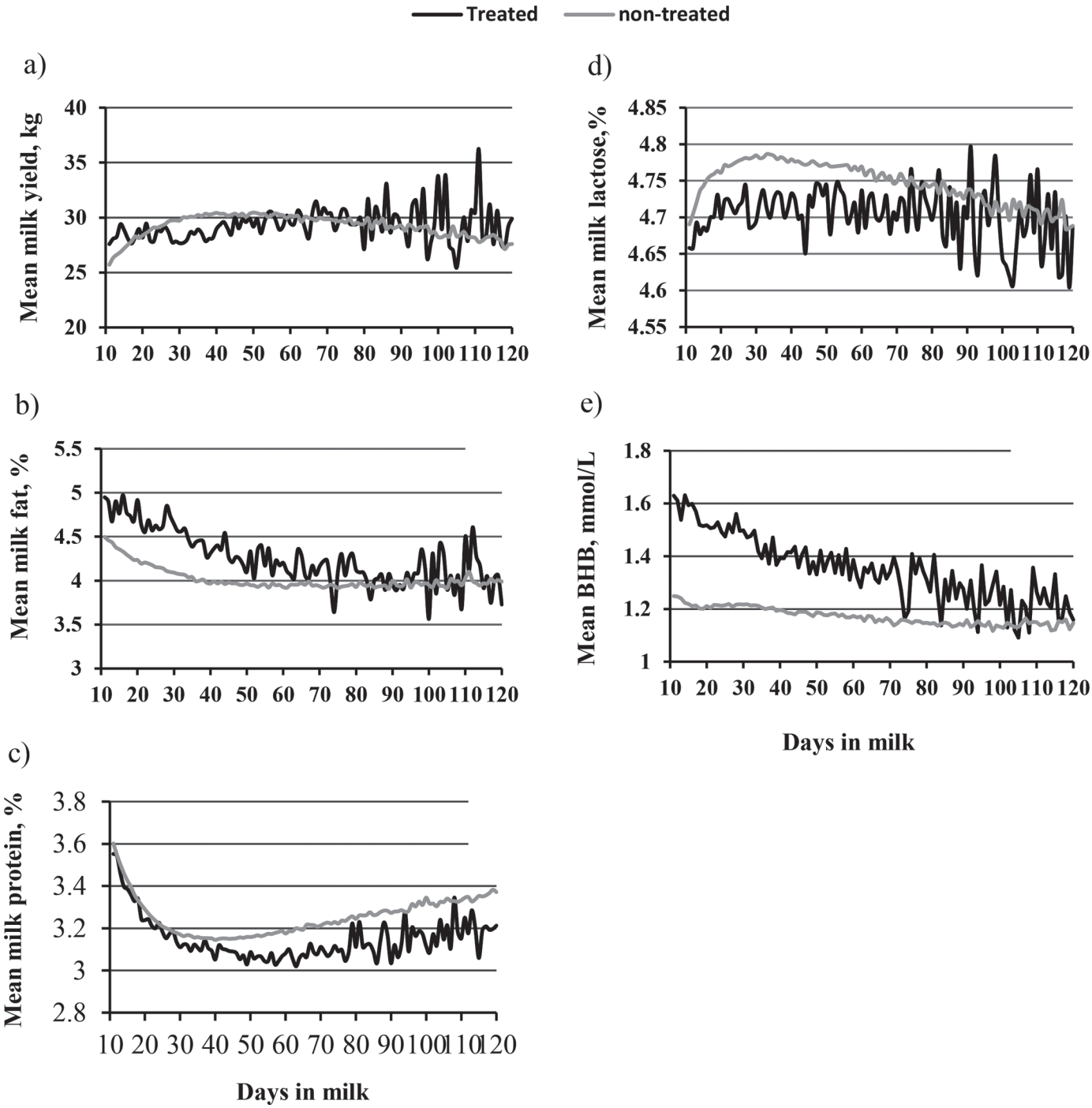

Figure 4. Mean (a) milk yield, (b) milk fat content, (c) milk protein content, (d) lactose content, and (e) blood BHB predicted from milk spectra by DIM for healthy cows (not treated for ketosis) and cows treated by veterinarian for clinical ketosis within the first 120 d after calving.

Table 3. Means (SD) of blood BHB predicted from milk spectra at 11 to 30 (BHB_1), 31 to 60 (BHB_2), 61 to 90 (BHB_3), and 91 to 120 DIM (BHB_4) and across early lactation stage (11 to 120 DIM; BHB_{all}) for nontreated cows or cows treated for clinical ketosis based on data set 3

Trait	Period, DIM	Clinical ketosis	
		Nontreated	Treated
BHB_1	11–30	1.218 (0.330)[b]	1.540 (0.374)[a]
BHB_2	31–60	1.193 (0.291)[b]	1.405 (0.342)[a]
BHB_3	61–90	1.155 (0.264)[b]	1.315 (0.297)[a]
BHB_4	91–120	1.141 (0.258)[b]	1.232 (0.295)[a]
BHB_{all}	11–120	1.195 (0.303)[b]	1.434 (0.359)[a]

[a,b]Values with different superscripts in the same row were significantly different at $P < 0.05$, which was tested by 2-sample t test.

mean milk lactose content from healthy cows decreased whereas that of treated cows stabilized at an average value of around 4.7% and slightly decreased in the last 20 DIM (Figure 4d).

Cows treated for KET showed much more variation of the means per DIM for all traits compared with nontreated cows (Figure 4). This is due to the smaller number of observations for treated cows (7,000) compared with nontreated cows (350,000). This is also evident in early lactation where, for treated cows, variation was smaller than in later lactation stages in all traits. This is because more animals were treated in early lactation. As DIM progressed the number of cows treated was reduced, resulting in larger variation in means per DIM.

Heritability

Table 4 shows estimates of variance components and corresponding variance ratios of predicted blood BHB traits from univariate analyses. The estimated heritability of predicted blood BHB across lactation stages (11–120 DIM) was moderate (0.274); that of predicted blood BHB at different DIM intervals increased with lactation stage from 0.250 for BHB_1 to 0.365 for BHB_4, with standard errors ranging from 0.004 to 0.006 (Table 4). The heritability estimates of predicted blood BHB at different stages were similar in univariate and bivariate analyses [BHB at different DIM intervals with each other (Table 5) or with milk production traits]. In data set 3, however, heritability estimates of predicted blood BHB from bivariate analyses with KET were slightly lower (0.238 to 0.353), with relatively higher standard errors (0.006 to 0.008). The medium heritability of predicted blood BHB suggests that genetic selection for lower blood BHB concentrations in early lactation (<120 DIM) is feasible and may lower occurrences of ketosis. In agreement with the current study, Koeck et al. (2014) found an increasing trend in heritability for milk BHB with DIM, but Oikonomou et al. (2008) obtained a decreasing trend in heritability of measured serum BHB as DIM increased in primiparous cows. In the literature, estimates of heritabilities vary from 0.08 to 0.40 for measured blood BHB (Oikonomou et al., 2008; van der Drift et al., 2012b) and from 0.067 to 0.29 for milk BHB (van der Drift et al., 2012b; Koeck et al., 2014; Jamrozik et al., 2016). The heritability estimates of predicted blood BHB traits found in our study were generally in the range of published values, but slightly higher especially for BHB after 60 DIM. Among other factors, differences in periods of lactation (11–120 DIM vs. 5–60 or 100 DIM) and definitions of BHB traits might contribute to the differences in estimates.

Variance components and corresponding variance ratios of registered clinical KET across lactations from univariate analyses are given in Table 4. The heritability estimate of KET in univariate analysis based on data set 2 was 0.078 (Table 4), but was reduced to 0.002 when KET was analyzed bivariately either with predicted blood BHB traits (Table 7) or milk production traits using data set 3 (Table 8). As estimates of heritability for binary traits with linear models are frequency-dependent, the reduction in heritability of KET in bivariate analysis could be due to the low frequency of KET in data set 3 compared with that

Table 4. Estimates of additive genetic $\left(\sigma_a^2\right)$, permanent animal environment $\left(\sigma_{pe}^2\right)$, herd test day or herd year $\left(\sigma_{htd}^2\right)$ and residual $\left(\sigma_e^2\right)$ variances, as well as variance ratios for genetic (h^2), permanent environment (c^2), herd test day or herd year (d^2), and residual (e^2) effects for blood BHB predicted from milk spectra at 11 to 30 (BHB_1), 31 to 60 (BHB_2), 61 to 90 (BHB_3), 91 to 120 (BHB_4), and 11 to 120 DIM (BHB_{all}) and clinical ketosis (KET) from univariate analyses based on data set 1 for BHB and data set 2 for KET[1]

Trait	σ_a^2	σ_{pe}^2	σ_{htd}^2	σ_e^2	h^2	c^2	d^2	e^2
BHB_1	0.023564	0.010366	0.015343	0.044974	0.250	0.110	0.163	0.477
BHB_2	0.020551	0.007571	0.014075	0.031134	0.280	0.103	0.192	0.425
BHB_3	0.020069	0.005571	0.012503	0.023387	0.326	0.091	0.203	0.380
BHB_4	0.021047	0.004334	0.012248	0.020069	0.365	0.075	0.212	0.384
BHB_{all}	0.019683	0.005257	0.013237	0.033719	0.274	0.073	0.184	0.469
KET[2]	0.001571	0.001017	0.001138	0.016472	0.078	0.050	0.056	0.816

[1]Standard error for $h^2 = 0.003$–0.006; for $c^2 = 0.002$–0.006; for $d^2 = 0.001$–0.003; and for $e^2 = 0.002$–0.006.

[2]For KET, σ_{htd}^2 and d^2 represent herd-year variance and the corresponding variance ratio, respectively.

Table 5. Heritabilities[1] (bold, on diagonal), genetic correlations (above diagonal), and phenotypic correlations (below diagonal) with SE in parentheses for BHB predicted from milk spectra at 11 to 30 (BHB_1), 31 to 60 (BHB_2), 61 to 90 (BHB_3), and 91 to 120 (BHB_4) from bivariate analyses of data set 1

Trait	BHB_1	BHB_2	BHB_3	BHB_4
BHB_1	**0.248 (0.005)**	0.922 (0.007)	0.830 (0.009)	0.763 (0.011)
BHB_2	0.489 (0.003)	**0.274 (0.004)**	0.975 (0.003)	0.949 (0.004)
BHB_3	0.451 (0.003)	0.574 (0.002)	**0.322 (0.005)**	0.977 (0.003)
BHB_4	0.413 (0.003)	0.541 (0.002)	0.619 (0.002)	**0.360 (0.005)**

[1]Heritability estimate and the corresponding SE in parentheses were calculated as the average estimate from all bivariate analyses containing a particular trait.

in data set 2. Estimates of heritability from univariate analysis for KET were in agreement with previous estimates from linear models (0.01 to 0.08; Jamrozik et al., 2016; Koeck et al., 2016; Pryce et al., 2016), but lower than the majority of estimates from threshold models (0.02 to 0.16; Pryce et al., 2016). Heringstad et al. (2005) obtained substantially higher estimates for KET on the same population (NRF) with threshold models, with estimates of 0.14, 0.15, and 0.16 for first, second, and third lactations, respectively. However, it has to be noted that linear model estimates of heritability for binary traits are frequency-dependent and therefore not directly comparable with estimates on the underlying liability scale (Pryce et al., 2016).

Proportion of Variance Attributed to PE, HTD, or HY

The proportion of variance attributed to PE, HTD, and residual for predicted blood BHB traits are also given in Table 4. The HTD variance was lower than the additive genetic variance and the proportion of variance attributed to HTD increased as DIM progressed, from 16 to 21%. This indicates that events on test days (e.g., feeding and management) have less influence on the etiology of ketosis than genetic difference between cows. In contrast, van der Drift et al. (2012b) found a larger proportion of variance attributed to herd (not to HTD) than that of additive genetic variance for plasma BHB. Though effects of HTD were smaller than additive genetic effects, they had considerable influences (explained 16 to 21% of variation) on BHB traits. Therefore, prevention strategies for ketosis should include both feeding and management strategies at dairy farms, and genetic improvement through breeding programs, which was also concluded by van der Drift et al. (2012b). Similar to HTD effects, the proportion of variance attributed to PE was smaller than that of additive genetic variance, and it decreased as DIM progressed, from 11 to 7.5% of the total variance. In the study of Jamrozik et al. (2016), the permanent environmental effect captured 25% of the total variance in milk BHB in later lactations, which is more than 2 times the estimates found in the current study.

For KET, the proportion of variance attributed to HY, PE, and residual are presented in Table 4. The proportion of variance attributed to HY was slightly lower than that of additive genetic variance (5.6 vs. 7.8%) for univariate analysis. However, in bivariate analysis, the proportion of variance attributed to HY was much larger (87.4%) than that of additive genetic variance (results not shown in table). This result suggests that environmental factors (feeding and management) have more influence on the prevalence of KET in HY than the genetic difference between cows. Estimates of the HY effect obtained in the current study were higher than estimates reported for HY effects in Canadian Holsteins (Jamrozik et al., 2016). For KET and its indicator (predicted blood BHB), estimates of residual effects were lower than values reported in literature (Jamrozik et al., 2016), indicating that the models used in the current study fit well.

Genetic and Phenotypic Correlations Among BHB Traits

Estimates of genetic and phenotypic correlations among predicted blood BHB traits are given in Table 5. The genetic correlations between the predicted blood BHB traits were higher between adjacent DIM intervals (0.92–0.98) and decreased as intervals were further apart (down to 0.76). This is in agreement with results found by Koeck et al. (2014) for milk BHB traits defined in a 20-d interval for cows between 5 and 60 DIM. Similar to the genetic correlations, the estimates of phenotypic correlations were higher between adjacent DIM intervals and in line with Koeck et al. (2014). Genetic correlations were strongest between BHB_2 and BHB_3 as well as BHB_3 and BHB_4, whereas phenotypic correlation was the strongest between BHB_3 and BHB_4 (0.62).

Genetic and Phenotypic Correlations Among BHB, Milk Traits, and KET

Genetic correlations of predicted blood BHB traits with milk production traits from the same lactation

Table 6. Estimates of heritability[1] (h^2) and genetic (r_g) and phenotypic (r_p) correlations (SE) of blood BHB predicted from milk spectra at 11 to 30 (BHB_1), 31 to 60 (BHB_2), 61 to 90 (BHB_3), and 91 to 120 (BHB_4) with milk production traits[2] from the same lactation stage as BHB based on data set 1 in bivariate analyses

	11–30 DIM			31–60 DIM			61–90 DIM			91–120 DIM		
Trait[2]	h^2	r_g	r_p	h^2	r_g	r_p	h^2	r_g	r_p	h^2	r_g	r_p
BHB_{1-4}	0.249			0.285			0.329			0.363		
	(0.006)			(0.005)			(0.005)			(0.005)		
Milk, kg	0.164	0.188	0.108	0.190	0.086	0.042	0.214	0.049	0.020	0.229	0.063	−0.001
	(0.006)	(0.023)	(0.003)	(0.005)	(0.017)	(0.002)	(0.005)	(0.016)	(0.003)	(0.006)	(0.015)	(0.003)
Fat, kg	0.106	0.273	0.405	0.105	0.110	0.347	0.108	0.037	0.298	0.127	0.045	0.25
	(0.005)	(0.024)	(0.002)	(0.004)	(0.020)	(0.002)	(0.004)	(0.020)	(0.002)	(0.005)	(0.019)	(0.002)
Prot, kg	0.131	0.108	0.013	0.160	−0.067	−0.083	0.177	−0.129	−0.111	0.185	−0.106	−0.122
	(0.006)	(0.025)	(0.003)	(0.005)	(0.018)	(0.002)	(0.005)	(0.017)	(0.003)	(0.005)	(0.016)	(0.003)
Lact, kg	0.141	0.125	0.066	0.174	0.032	0.008	0.202	0.002	−0.013	0.221	0.019	−0.033
	(0.006)	(0.024)	(0.003)	(0.005)	(0.018)	(0.002)	(0.005)	(0.016)	(0.003)	(0.006)	(0.016)	0.003
Fat, %	0.096	0.168	0.445	0.105	0.062	0.421	0.122	−0.006	0.380	0.167	−0.030	0.351
	(0.005)	(0.026)	(0.002)	(0.004)	(0.020)	(0.002)	(0.004)	(0.019)	(0.002)	(0.005)	(0.017)	(0.002)
Prot, %	0.272	−0.233	−0.255	0.383	−0.272	−0.307	0.441	−0.280	−0.311	0.318	−0.278	−0.297
	(0.007)	(0.018)	(0.003)	(0.005)	(0.012)	(0.002)	(0.005)	(0.011)	(0.002)	(0.002)	(0.004)	(0.003)
Lact, %	0.406	−0.234	−0.200	0.451	−0.172	−0.167	0.458	−0.159	−0.163	0.455	−0.154	−0.167
	(0.007)	(0.016)	(0.003)	(0.005)	(0.012)	(0.002)	(0.005)	(0.011)	(0.002)	(0.006)	(0.011)	(0.003)

[1]Heritability estimates for blood BHB traits and the corresponding standard error in parentheses were calculated as the average estimate from all bivariate analyses containing a particular trait.

[2]Prot = protein yield (kg) or protein content (%); Lact = lactose yield (kg) or lactose content (%).

stage as BHB (Table 6) were slightly different from the correlation estimates with milk production traits across lactation stages (Table 7). For example, fat yield and fat and lactose contents at 11 to 30 DIM and protein content at 61 to 90 and 91 to 120 DIM from the same lactation stage as BHB had slightly stronger genetic correlations with BHB than corresponding estimates for those milk traits across lactation stage with BHB traits. Predicted blood BHB at the first test-day (BHB_1) was genetically moderately correlated with milk production traits both from the same lactation stage (Table 6) and across lactation stages (Table 7), except for milk fat content that was weakly correlated (Table 7). All predicted blood BHB traits were moderately negatively correlated with milk protein and lactose contents (Tables 6 and 7). The remaining milk traits showed negligible genetic correlation with predicted blood BHB in later lactation stages (31–120 DIM), except for milk and fat yields with BHB_2 and protein yield with BHB_3 and BHB_4 (Tables 6 and 7). Similar to genetic correlations, phenotypic correlations of BHB traits with milk production traits decreased as DIM progressed. Predicted blood BHB traits had moderate negative phenotypic correlations with milk protein and lactose contents from the same lactation stage (Table 6) and across lactation stages (Table 7). Unlike the genetic correlations, phenotypic correlations of BHB traits with milk traits from the same lactation stage as BHB were stronger than estimates across lactation stages. Predicted blood BHB traits were more strongly phenotypically correlated with fat content from the same lactation stage (0.351–0.445; Table 6) than across lactation stages (0.175–0.403; Table 7).

To the best of our knowledge, estimates of genetic and environmental correlations between milk or blood BHB and milk production traits are not available in the literature, except the work of Koeck et al. (2014), who reported correlations between EBV for milk BHB traits and routinely evaluated traits including yields of milk, fat, and protein. In agreement with the current study, Koeck et al. (2014) found moderate correlations (0.13–0.22) between EBV of milk BHB and milk yields, but found insignificant ($P > 0.05$) correlations between EBV of milk BHB and yields of fat and protein. The present results indicate higher genetic merits for milk, fat, protein, and lactose yields associated with higher BHB in early lactation and, therefore, a greater susceptibility to risk of ketosis. Phenotypic associations between predicted blood BHB and milk traits are given in Figure 3. They show, for example, that cows that had high milk yield in early lactation (up to 60 DIM) had positive test for risk of ketosis (high BHB values; Figure 3a). The opposite was true for cows with high milk protein content throughout all lactation stages considered

Table 7. Estimates of heritability[1] (h^2), genetic correlations (r_g), and phenotypic correlations (r_p) of blood BHB predicted from milk spectra at 11 to 30 (BHB_1), 31 to 60 (BHB_2), 61 to 90 (BHB_3), 91 to 120 (BHB_4), and 11 to 120 DIM (BHB_{all}) with clinical ketosis (KET) and milk production traits across lactation stage from bivariate analyses

Parameter	Trait	h^2	BHB_1	BHB_2	BHB_3	BHB_4	BHB_{all}
r_g	KET	0.002 (0.0002)	0.469 (0.050)	0.310 (0.049)	0.192 (0.049)	0.179 (0.048)	0.288 (0.043)
	Milk, kg	0.195 (0.003)	0.277 (0.016)	0.118 (0.014)	0.024 (0.013)	−0.031 (0.013)	0.101 (0.010)
	Fat, kg	0.107 (0.002)	0.248 (0.016)	0.126 (0.015)	0.069 (0.015)	−0.011 (0.014)	0.106 (0.011)
	Protein, kg	0.165 (0.003)	0.107 (0.017)	−0.047 (0.014)	−0.124 (0.014)	−0.166 (0.013)	−0.052 (0.011)
	Lactose, kg	0.181 (0.003)	0.229 (0.016)	0.063 (0.013)	−0.028 (0.013)	−0.081 (0.016)	0.051 (0.010)
	Fat, %	0.116 (0.002)	0.033 (0.016)	0.054 (0.014)	0.084 (0.014)	0.042 (0.013)	0.035 (0.011)
	Protein, %	0.371 (0.003)	−0.367 (0.011)	−0.308 (0.009)	−0.252 (0.009)	−0.215 (0.009)	−0.288 (0.007)
	Lactose, %	0.428 (0.003)	−0.189 (0.012)	−0.178 (0.009)	−0.173 (0.009)	−0.163 (0.009)	−0.174 (0.007)
r_p	KET		0.065	0.047	0.041	0.023	0.047
	Milk, kg		0.135 (0.002)	0.033 (0.002)	−0.013 (0.002)	−0.038 (0.002)	0.042 (0.002)
	Fat, kg		0.382 (0.002)	0.231 (0.002)	0.143 (0.002)	0.102 (0.002)	0.327 (0.001)
	Protein, kg		0.024 (0.003)	−0.065 (0.002)	−0.091 (0.002)	−0.107 (0.002)	−0.073 (0.001)
	Lactose, kg		0.096 (0.003)	0.005 (0.002)	−0.038 (0.002)	−0.062 (0.002)	0.009 (0.002)
	Fat, %		0.403 (0.002)	0.281 (0.002)	0.202 (0.002)	0.175 (0.002)	0.403 (0.001)
	Protein, %		−0.285 (0.002)	−0.238 (0.002)	−0.186 (0.002)	−0.165 (0.002)	−0.292 (0.001)
	Lactose, %		−0.188 (0.003)	−0.137 (0.002)	−0.126 (0.002)	−0.123 (0.002)	−0.173 (0.002)

[1]Heritability estimate for ketosis and milk traits and the corresponding standard errors in parentheses were calculated as the average estimate from all bivariate analyses containing a particular trait.

(Figure 3c). The genetic associations observed between yield traits and BHB concentrations were expected, as genetic selection for high milk production would result in larger negative energy balance and require larger fat mobilization in early lactation (Veerkamp et al., 2003; Coffey et al., 2004), and hence a higher risk of ketosis.

Estimates of genetic correlations of BHB traits with KET are also presented in Table 7. All BHB traits were genetically moderately correlated with KET, with correlations between 0.18 and 0.47. Genetic relationship between KET and its indicator (predicted blood BHB) was reduced as DIM progressed. Estimates of genetic correlations between KET and its indicator at 11 to 30 and 31 to 60 DIM were in the range of that reported in literature (Koeck et al., 2014; Koeck, 2015; Jamrozik et al., 2016). Koeck et al. (2014) found an estimate of genetic correlation between KET and milk BHB at 5 to 40 DIM of 0.48, which is comparable with the 0.47 estimate observed between KET and blood BHB at 11 to 30 DIM in the current study. Jamrozik et al. (2016) found a genetic correlation of KET with milk BHB, with correlations of 0.63 and 0.37 for first and later lactations, respectively, and with a correlation of 0.25 for both KET and milk BHB in the later lactations. However, Koeck (2015) and Koeck et al. (2016) reported stronger genetic correlation between KET and milk BHB at 5 to 40 DIM, with correlations ranging from 0.70 to 0.75. Phenotypic correlations were low between KET and blood BHB traits, ranging from 0.023 (between KET and BHB_4) to 0.065 (between KET and BHB_1; Table 7), which is much lower than estimates reported for phenotypic correlations between KET and milk BHB at 5 to 40 DIM (0.150 to 0.186; Koeck et al., 2014, 2016).

Table 8. Estimates of heritability[1] (h^2), genetic (r_g), and phenotypic (r_p) correlations of clinical ketosis (KET) with milk production traits from bivariate analysis based on data set 3

		KET	
Trait	h^2	r_g	r_p
KET	0.002 (0.0002)		
Milk, kg	0.183 (0.003)	0.178 (0.047)	−0.042
Fat, kg	0.103 (0.003)	0.157 (0.046)	−0.010
Protein, kg	0.156 (0.004)	0.002 (0.048)	−0.050
Lactose, kg	0.169 (0.004)	0.161 (0.048)	−0.046
Fat, %	0.114 (0.003)	−0.023 (0.049)	0.033
Protein, %	0.361 (0.003)	−0.333 (0.039)	−0.017
Lactose, %	0.412 (0.003)	−0.043 (0.037)	−0.025

[1]Heritability estimate for ketosis and the corresponding standard error in parentheses were calculated as the average estimate from all bivariate analyses containing a particular trait.

Table 8 presents the estimates of genetic and phenotypic correlations between KET and milk productions. Ketosis was significantly positively correlated with milk (0.178), fat (0.157), and lactose (0.161) yields, but not genetically correlated with protein yield (0.002). Previous studies on genetic correlations between KET and milk production traits in early lactation are scarce. Koeck et al. (2013) found that genetic correlations between milk yield at 5 to 30 and 31 to 60 DIM with KET were not different from zero. In their comprehensive review, Pryce et al. (2016) indicated that mean genetic correlation between 305-d milk yield and KET was unfavorable (positive), which is in line with the current study. In the same review, negative mean genetic correlations between KET and 305-d fat and protein yields

were reported (Pryce et al., 2016). In the current study, none of the genetic correlations of KET with milk fat (−0.023) or lactose (−0.043) content were significantly different from zero, but with milk protein content it was (−0.333). Contrary to the current finding, Koeck et al. (2013) reported a near zero genetic correlation of KET with milk protein content (−0.06 at 5–30 DIM and −0.09 at 31–60 DIM), but a medium positive genetic correlation with milk fat content at 5 to 30 DIM (0.33). The genetic relationships between KET and milk production traits observed in the current study indicated that a higher milk, fat, and lactose yields and a lower milk protein content would be associated with an increased risk of developing ketosis.

Phenotypic correlations between KET and milk production traits were low and negative (except for fat content that had a low positive genetic correlation with KET). This is in agreement with the phenotypic correlations of KET with milk yield and fat and protein contents reported by Koeck et al. (2013).

CONCLUSIONS

Blood BHB predicted from milk spectra at different DIM intervals or across lactation stages is heritable, with heritability estimates ranging from 0.250 to 0.365. It seems sufficient to consider only BHB_1 and BHB_2 as indicator traits in a routine genetic evaluation for resistance to ketosis because BHB_1 and BHB_2 are available early in lactation and have higher genetic correlations with KET than later BHB traits (BHB_3 and BHB_4). Generally, predicted blood BHB was genetically moderately correlated with KET and milk production traits, and those correlations decreased as DIM progressed. Similarly, KET had moderate genetic correlations with milk, fat, and lactose yields and protein content. The moderate genetic correlations observed between BHB traits and KET indicate that selective breeding for lower BHB may contribute to lower susceptibility of cows to ketosis in early lactation. A lower BHB was genetically associated with higher milk protein and lactose contents, but with lower milk, fat, lactose, and protein yields. Blood BHB predicted from milk spectra can be routinely obtained from test-day milk samples and provides a practical alternative for breeding cows to have lower susceptibility to ketosis, even though correlations with KET are moderate. Before commencing genetic selection for a lower BHB in NRF dairy cattle, further studies are needed on genetic associations of BHB with health and fertility traits. The benefit of using FT-MIR predicted indicator trait (e.g., BHB) in addition to the directly observed ketosis also has to be studied.

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