Genetic parameters for endocrine and traditional fertility traits, hyperketonemia and milk yield in dairy cattle

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Short title: Fertility and hyperketonemia in dairy cattle

Abstract

High-yielding cows may suffer from negative energy balance during early lactation, which can lead to ketosis and delayed ability of returning to cyclicity after calving. Fast recovery after calving is essential when breeding for improved fertility. Traditionally used fertility traits, such as the interval from calving to first insemination (CFI), have low heritabilities and are highly influenced by management decisions. Herd Navigator™ management program samples and analyses milk progesterone and β-hydroxybutyrate (BHB) automatically during milking. In this study, the genetic parameters of endocrine fertility traits (measured from milk progesterone) and hyperketonemia (measured from milk BHB) in early lactation were evaluated and
compared with traditional fertility traits (CFI, interval from calving to the last
insemination and interval from first to last insemination) and the milk yield in red dairy
cattle herds in Finland. Data included observations from 14 farms from 2014 to 2017.
Data were analysed with linear animal models using DMU software and analyses were
done for first parity cows. Heritability estimates for traditional fertility traits were low and
varied between 0.03 and 0.07. Estimated heritabilities for endocrine fertility traits
(interval from calving to the first heat (CFH) and commencement of luteal activity (C-LA)) were higher than for traditional fertility traits (0.19-0.33). Five slightly different
hyperketonemia traits divided into two or three classes were studied. Linear model
heritability estimates for hyperketonemia traits were low, however when the threshold
model was used for binary traits the estimates became slightly higher (0.07-0.15).
Genetic correlation between CFH and C-LA for first parity cows was high (0.97) as
expected since traits are quite similar. Moderate genetic correlations (0.47-0.52) were
found between the endocrine fertility traits and early lactation milk yield. Results
suggest that the data on endocrine fertility traits measured by automatic systems is a
promising tool for improving fertility, specifically when more data is available. For
hyperketonemia traits, dividing values into three classes instead of two seemed to work
better. Based on the current study and previous studies, where higher heritabilities
have been found for milk \( \beta \)-hydroxybutyrate traits than for clinical ketosis, milk \( \beta \)-
hydroxybutyrate traits are a promising indicator trait for resistance to ketosis and
should be studied more. It is important that this kind of data from automatic devices is
made available to recording and breeding organizations in the future.

**Keywords:** progesterone, ketosis, \( \beta \)-hydroxybutyrate, heat detection, nordic red
Implications

The genetic parameters of endocrine fertility traits (measured from milk progesterone) and hyperketonemia (measured from milk $\beta$-hydroxybutyrate) in early lactation were evaluated and compared with traditional fertility traits and the milk yield in dairy cattle. Traditional fertility traits are commonly used in breeding schemes even though they are highly influenced by management decisions and have low heritabilities. Heritability estimates for endocrine fertility traits were higher than for traditional fertility traits, consequently data on fertility traits measured by automatic systems is a promising tool for improving fertility, specifically when more data is available. For hyperketonemia traits, heritability estimates were quite low.

Introduction

Good fertility is an important determinant of dairy production efficiency. Nordic total merit (NTM) aims for healthy, fertile, well producing and long-lasting cows (NAV, 2018). For red dairy cattle (RDC), the relative weight for yield represents currently about 33% of the total merit. The correlation between yield index and NTM is 0.63, while the correlation between fertility index and NTM is 0.22. Hence considerably greater genetic response can be expected on production traits. Many previous studies have shown an unfavorable genetic correlation between milk production and fertility traits (e.g. Berry et al., 2014). Detecting the heats and inseminating the cows at the correct time is crucial for achieving high conception rates. In addition, high yielding cows are susceptible to ketosis, a metabolic disorder, which has been associated to descended health, fertility and milk production (e.g. Duffield, 2009). Insemination measurements, such as the interval from calving to the first insemination, are generally used to evaluate cow’s ability of returning to cyclicity after calving. However, insemination traits
are highly influenced by management decisions and tend to have low heritabilities (e.g. Berry et al., 2014). Instead, endocrine fertility traits are more accurate and have been found to have higher heritabilities than traditional fertility traits (Royal et al., 2002; Petersson et al., 2007).

DeLaval Herd Navigator™ (HN, DeLaval International, Tumba, Sweden) management program samples and analyses four biological parameters (progesterone, β-hydroxybutyrate, lactate dehydrogenase and urea) in milk automatically during milking. HN uses frequent progesterone (P4) measurements to determine the reproduction status of the cow and detect the heat. If frequent P4 measurements are used, heat can be identified accurately even if the cow is not showing any visible signs of heat. Progesterone is sampled at varying intervals depending on the cow’s estrus cycle (Friggens et al., 2008).

Hyperketonemia or ketosis is primarily found in early lactation and is caused by a severe negative energy balance. In subclinical ketosis, no clinical signs can be seen but ketone body concentrations, such as β-hydroxybutyrate (BHB), increase in the blood, urine and milk (e.g. Koeck et al., 2014). Concentrations of BHB in the blood have been used to diagnose hyperketonemia (Duffield, 2009) but this procedure is not practical and suitable for routine analysis. Previous studies have shown a high correlation between blood and milk BHB (Denis-Robichaud et al., 2014) and that milk BHB is a useful tool for diagnosing hyperketonemia (e.g. Koeck et al., 2014). In previous studies, lower conception rates have been found for cows with larger BHB concentrations than for healthy cows (e.g. Blom et al., 2015). The incidence of clinical ketosis is low in Finland, in a study by Rajala-Schultz et al. (1999) the incidence for
Finnish Ayrshire was 3.3% and in the 2016 national dairy cattle health recording results (treatments by veterinarians) even lower being 1.04% (Faba, 2017). However, subclinical ketosis is more common, is not recorded, and can be costly to farmers as it has a negative effect on cows overall performance (Duffield et al., 2009).

Traditional fertility traits and clinical ketosis are currently included in the Nordic breeding goal. For fertility traits, interval from calving to the first insemination (CFI), interval from first to last insemination (IFL), number of inseminations, non-return rate, conception rate and heat strength (data only from Sweden) are included, the heritability estimates for these traits are very low varying from 0.015 to 0.04 for first parity RDC cows. Heritability for clinical ketosis is 0.01 for first parity RDC cows.

The objective of this study was to estimate the genetic parameters of endocrine (P4) fertility traits and hyperketonemia (measured from milk BHB concentrations) in early lactation measured by the HN system and compare these traits with the traditional fertility traits (CFI, interval from calving to the last insemination (CLI) and IFL) and milk yield in Nordic RDC herds in Finland.

Materials and Methods

In this study HN data from P4 and BHB concentrations from 14 Finnish dairy farms were provided by Lattec I/S (Hillerød, Denmark). Data were available from 2014 to 2017 although for 6 herds data was available from 2015 onwards and for 3 herds only from 2016. Milk P4 data (17-365 days postpartum) included 2531 observations from 1622 RDC cows from parities 1-3. Some of the cows had records from multiple parities and the average number of observations per herd was 181 (range 15-795). For
endocrine fertility traits, early lactation observations within 100 days postpartum were included in the analysis. In this dataset, many cows which had observation for the second and / or third parity were missing the first parity record due to recent investment to HN. Including animals with only later parity records can lead to biased estimates of genetic parameters, since information on selection process is missing. Therefore, genetic analyses were performed only for the first parity cows in this study.

HN starts to record and analyze P4 concentrations from ca. 20 days after calving and uses immunoassay based dry-stick technique (Samsonova et al., 2015). An extended Kalman filter is used to smooth the raw P4 values and a biological model is applied to predict the cows’ reproduction status (Friggens et al., 2008). Cows are classified to three categories based on their reproduction status (0 = postpartum anestrus, 1 = oestrus cycling and 2 = potentially pregnant), additionally time (days) to the next sample (DNS) is defined based on the reproduction status (Friggens et al., 2008). Two P4 traits were studied, days from calving to the first heat (CFH, restricted to ≤100 days) identified by HN system and days from calving to luteal activity (C-LA, restricted to ≤100 days). C-LA was calculated as a reproduction status change from 0 to 1 or 2 and it is assumed to describe accurately the first real heat since it is measured within a few days after the first heat has occurred. The CFH is difficult to detect from the P4 curve, since the P4 concentrations tend to be constantly low after calving (Figure 1). Hence, the model identifies P4 concentration change from high to low, determines passed heat and will be searching for new heat from around 17 - 18 days later. Therefore, CFH is recorded when the progesterone concentration changes from high to low and it actually describes the second real heat after calving.
Insemination and pedigree data for the 14 HN farms studied were provided by Faba Coop (Vantaa, Finland). Three traditional fertility traits were analyzed, the interval (days) from calving to the first insemination (CFI, restricted to $\leq 230$ days), interval (days) from calving to the last insemination (CLI, restricted to $\leq 365$ days) and interval (days) from first to last insemination (IFL). Two different datasets with different trait groups were created, first dataset included CFH and traditional fertility traits (CFI, CLI, IFL) and second dataset had observations for CFH, C-LA, milk yield (5 to 70 days postpartum) and two ketosis traits derived from smoothed BHB values (5 to 60 days postpartum).

For first parity cows, smoothed BHB values, based on prior measurements, between 5 and 60 days postpartum were used in the analysis. Cows (16 animals) with less than 4 BHB records were removed after which total of 16 851 observations from 794 first parity cows remained. The mean number of observations were 21.2 (range 4-55). Two BHB traits were defined which divided observations into three levels (0/1/2) with slightly different BHB thresholds (ket_s1 and ket_s2) to describe the cows’ hyperketonemia status. In ket_s1 the value “negative” implied that milk BHB $< 0.10$ mmol/l; animals with $0.10 \leq$ milk BHB $< 0.20$ mmol/l were “suspect” and animals with milk BHB $\geq 0.20$ mmol/l were “positive”. Thresholds used for ket_s2 were: negative (milk BHB $< 0.15$ mmol/l), suspect ($0.15 \leq$ milk BHB $< 0.20$ mmol/l) or positive (milk BHB $\geq 0.20$ mmol/l). These thresholds were chosen based on the previous studies where BHB values between 0.10 and 0.20 mmol/l have been used (e.g. Denis-Robichaud et al., 2014; Koeck et al., 2014). Leblanc (2010) suggested that if individual cows are inspected instead of group-level monitoring 0.20 mmol/l threshold should be used, therefore also binary trait (0/1 trait: ketosis_b) with a threshold of 0.20 mmol/l was studied. Only one, highest,
observation per cow was used in the analysis. Because BHB baseline can vary among cows due to the diet (Nielsen et al., 2010) also two binary (0/1) traits (ket_r1 and ket_r2) based on the ketosis risk values calculated by HN were studied. HN calculates the risk of ketosis (value between 0 = no risk and 1 = clinical ketosis) with biological models and uses the cow level baseline of BHB (based on first few samples) in the calculations. Based on the literature, the thresholds selected for ketosis risk traits were 55 % for ket_r1 and 60 % for ket_r2 (e.g. Nielsen et al., 2005).

HN data included the information about milk yields from all milkings. The sum of milk yields from 5 to 70 days postpartum was used to study the early lactation milk yield. Cows with less than 60 milking records available were removed from the analysis (because of the fixed time frame of data collection, some cows had either missing beginning of the recording period or end of the period). Most of the cows had milking records for all days in the recording period but in the case of missing records the previous or following record was used in order to get 66 records for all cows. For example, if the recording period ended when cow was on 68 day postpartum the 68 day milk yield was used also for days 69 and 70.

Statistical analysis

Data were analysed with linear animal models using DMU software (Madsen and Jensen, 2013). Fixed effects were chosen based on the models used in Nordic cattle genetic evaluations and the structure of the data. Interactions (e.g. herd x year) were not included because of the small data size. Pedigree was traced 4 generations back. Univariate and multivariate models were used in genetic analyses. Univariate models were used for all traits in this study. Bivariate model was used to calculate the
correlation between endocrine fertility trait CFH and two traditional fertility traits which are included in the Nordic total merit (CFI, IFL). Multivariate models, with four traits at the time, were used to calculate the correlations between CFH, C-LA, milk yield and two ketosis traits derived from smoothed BHB values.

In matrix notation, the model was defined as follows:

\[ y = X\beta + Z_a a + e, \]

where \( y \) is a vector of observations; \( \beta \) is a vector of the fixed effects of herd, calving year, calving month (not for CLI and IFL), first insemination month (for CLI and IFL) and calving age; \( a \) is a vector of random animal effects. For single trait analysis \( a \sim N(0, A \sigma_a^2) \) where \( A \) is the additive genetic relationship matrix among animals and \( \sigma_a^2 \) is the additive genetic variance and \( e \) is a vector of random residuals \( e \sim N(0, I \sigma_e^2) \) where \( I \) is the identity matrix and \( \sigma_e^2 \) is the residual variance. \( X \) and \( Z \) are the corresponding incidence matrices. Calving age was divided into 7 classes <24, 24, 25, 26, 27, 28, >28 months.

In multivariate analysis, the variance-covariance structure for animal effects were defined as \( G = A \otimes G_0 \), where \( G_0 \) denotes the additive genetic variances and covariance’s between animal effects, \( \otimes \) the Kronecker product, and \( A \) is the additive genetic relationship matrix. Because not all animals had all records available the variance-covariance structures for residual effects were defined as a block-diagonal matrix \( R = \text{diag}(R_i) \), where \( R_i \) is the animal specific submatrix depending on the number of available records.

To remove the dependency with the incidence levels, the linear model heritability estimates from binary hyperketonemia traits were converted to underlying scale using
Dempster and Lerner (1950) approximation. In hyperketonemia analysis, also a
threshold model, using same fixed and random factors as in the linear model, was
tested to model binary traits using logit and probit link functions. The heritability
estimates for the logit model were calculated using the correction of the residual
variance by $\pi^2/3$, which is the variance of standard logistic distribution.

Results

The means for traditional fertility traits and CFH increased together with the parity
(Table 1). For C-LA the mean number of days were 39.8 (n=766), 37.7 (n=694) and
40.6 (n=473) for parities 1, 2 and 3, respectively. Most of the cows were inseminated
first time to the second heat identified by the HN system (First 17.3%, Second 31.2%
and Third 18.5%). The descriptive statistics for endocrine fertility traits and early
lactation milk yield used in multivariate analysis with hyperketonemia traits for first
parity cows are shown in Table 2. Distribution of the BHB values in hyperketonemia
trait classes are shown in Table 3.

Heritability estimates, analysed with univariate models, for traditional fertility traits were
low and varied between 0.03 and 0.07 in first parity cows (Table 4). The heritability
estimates for endocrine fertility traits were higher (Table 5). For first parity cows, the
heritability estimates for CFH were 0.19 and 0.33 in univariate and multivariate models,
respectively (Table 5). For C-LA, the univariate model heritability estimate for first
parity cows (n=766) was 0.24 (Table 5). The heritability estimate for 70 days
postpartum milk yield was as expected being 0.29 and 0.30 in the univariate and
multivariate analysis, respectively.
Linear model heritability estimates for ket_s1 and ket_s2 varied between 0.07 and 0.10 and were quite similar in univariate and multivariate analysis (Table 5). The heritability estimates for other hyperketonemia traits were also low (Table 6). Spearman’s rank correlation between ket_s1 and ket_s2, when animals were ordered based on their BLUP predictions, was very high (0.995). Spearman’s rank correlation between ket_r1 and ket_r2 was 0.988 and among the ketosis (ket_s1 and ket_s2) and risk level (ket_r1 and ket_r2) traits varied from 0.950 to 0.961.

Correlations between the endocrine and traditional fertility traits were positive and favorable. Genetic correlation between CFH and CFI was 0.12±0.55 and between CFH and CLI 0.33±0.54 for first parity cows. Correlation between CFH and C-LA for first parity cows was very high and favorable, genetic correlation being 0.97±0.02 and phenotypic correlation being 0.92 (Table 7). The unfavorable moderate genetic correlations were found between 5 to 70 days postpartum milk yield and endocrine fertility traits (Table 7). Genetic correlations between ket_s1 and endocrine fertility traits (CFH, C-LA) were small, negative and had high standard errors (Table 7). Unfavorable and quite high genetic correlation was found between ket_s1 and postpartum milk yield, however the estimate had a high standard error (0.59±0.39). Correlations for ket_s2 with endocrine fertility traits and milk yield were similar than for ket_s1.

Discussion

The overall mean for C-LA in first parity cows was 39.9 days which is close to one Tenghe et al. (2015) found for Holstein-Friesian cows in the Netherlands. (38.1 days). Bullman and Lamming (1978) indicated that C-LA occurs ca. 5 days after ovulation and
can be used to study the interval from calving to first ovulation. Based on previous results, the first ovulation occurred ca. 35 days postpartum in our study. In addition, shorter mean C-LA figures of 24.7-33.8 days have been reported in previous studies (e.g. Bullman and Lamming, 1978; Petersson et al., 2007). Differences between the figures may be due to different breeds, feeding practices, data editing and recording practices. For example, in HN herds the recording of P4 starts 20 days postpartum, whereas in some studies recording can start as early as 10 days postpartum. In addition, previous studies have indicated that declined dairy fertility and population differences can affect the length of this period (e.g. Pollott and Coffey, 2008).

In general, traditional fertility traits such as CFI has been used to evaluate cow’s ability of returning to cyclicity and these traits tend to have low heritabilities. In the current study, heritability estimates for traditional fertility traits were low and in similar magnitude than in previous studies. For example, Muuttoranta et al. (2015) found slightly lower heritability estimates for traditional fertility traits in RDC (0.03 for CFI and 0.02 for IFL) and Tenghe et al. (2015) reported slightly higher heritability for CFI (0.11±0.06) in Holstein-Friesian cows. The length of the voluntary waiting period and the visual checks of heats can differ widely among herds which can have an effect on the heritability estimates and lower the accuracy of the traditional fertility traits in dairy genetic evaluations.

In this study, estimated heritabilities for endocrine fertility traits (CFH and C-LA) were higher than for traditional fertility traits (0.19-0.33). Because of the small number of animals in the data, some of the estimates had high standard errors indicating limited accuracy of the estimates. The difference between the heritability estimates for CFH
between the univariate and multivariate model (0.19 and 0.33) were large most likely due to small data size, which is reflected by the standard errors of the estimates. It is also likely that with production information included the multi-trait models were better able to model the herd-year effects.

However, the magnitudes of the estimates are in line with previous studies where heritability estimates from 0.12 to 0.30 have been reported for endocrine fertility traits (e.g. Royal et al., 2002; Petersson et al., 2007; Tenghe et al., 2015). In addition, heritability estimates between 0.12 and 0.18 have been reported for traits based on cow activity, such as, calving to the first sign of high activity (CFHA) (Lovendahl and Chagunda, 2009; Ismael et al., 2015). Endocrine fertility traits reflect better cows’ reproductive physiology and tend to have higher heritabilities than traditional fertility traits and could therefore perform better in dairy breeding schemes. However, P4 are currently available only for the small number of cows and although activity measurements are widely used in management they are seldom collected to central data base. Before they can be used in the national genetic evaluations the recording of these traits should be done more commonly.

For hyperketonemia traits, linear model heritability estimates were low, however when the threshold model was used for binary traits or when the linear model estimates were transformed to the underlying scale the estimates became slightly higher (0.07-0.15). In a literature review, Pryce et al. (2016) reported low heritability estimates for clinical ketosis ranging from 0.01 to 0.16. In previous studies, most of the estimates for milk and serum BHB traits are low or moderate but higher than estimates for clinical ketosis (van der Drift et al., 2012; Koeck et al., 2014; Koeck et al., 2016; Miglior et al., 2014; Lee et al., 2016). For example, in a study of Lee et al. (2016) the heritability for milk
BHB 30 days postpartum was 0.10 (the average heritability for the first parity was 0.08).

In a study of Koeck et al. (2014) the heritability of milk BHB between 5 to 40 days postpartum was 0.14 and in a study of van der Drift et al. (2012) the heritability of milk BHB between 5 to 60 days postpartum was 0.16. In a study of Miglior et al. (2014) higher heritability estimates for milk BHB were found varying between 0.13 and 0.29 and increasing with days in milk. The differences in the estimates between studies can partly depend on the different traits used, for example maximum BHB concentration (e.g. Koeck et al., 2016), BHB concentration measured at first or some specific test day (e.g. van der Drift et al., 2012; Koeck et al., 2014; Lee et al., 2016) and classification based on different BHB thresholds (e.g. Miglior et al., 2014) have been used in previous studies. Most of the estimates found in literature are based on single or few BHB samples in the postpartum period. Although high sensitivity and specificity have been found in studies comparing milk and blood BHB measurements the use of single BHB values can be misleading if used to divide cows into ketotic or nonketotic since BHB levels can change considerably between days (Oetzl, 2007). In the current study, the frequent measurements of BHB were used which is deemed to be more accurate. There were only slight differences in the estimates, and Spearman’s rank correlations between predicted breeding values for different traits were high. The BHB baseline can vary between cows due to their dietary composition (Nielsen et al., 2010).

Risk level traits (ket_r1 and ket_r2) had lower heritability estimates than traits based on smoothed BHB concentrations and divided into three classes (ket_s1 and ket_s2), which was expected since continuous values contain more information. Based on the current study and previous studies, where higher heritabilities have been found for milk BHB traits than for clinical ketosis, it seems that including milk BHB traits as indicator traits to the national genetic evaluation for resistance to ketosis could be useful.
Identification of animals more susceptible to subclinical ketosis may provide additional ways to producers to reduce costs (e.g., subsequent decrease in health, fertility and production) that would not be identified if only using clinical ketosis.

Genetic correlation between CFH and C-LA for first parity cows was very high (0.97) as expected since both traits are measured from milk P4 concentration and describe the cow’s ability of returning to cyclicity after calving. No previous studies were found where these two traits were compared. Based on these results, both of the studied P4 traits can be used in genetic analysis when analyzing cow’s ability of returning to cyclicity after calving. In this study, CFH was chosen to be used in the multivariate analysis with traditional fertility traits and milk yield. Correlation between CFH and CFI (genetic 0.12±0.55, phenotypic 0.21) for first parity cows was lower than in many previous studies, however the standard error for this estimate was very high. In previous studies genetic correlations between 0.35 and 0.37 have been found among C-LA and CFI, however many of these estimates had high standard errors as well (e.g. Nyman et al., 2014; Tenghe et al., 2015). Positive genetic correlations indicate that selection for shorter C-LA will also reduce the interval for CFI. On the contrary, Royal et al. (2002) found a genetic correlation of -0.03±0.27 between the natural logarithm of milk C-LA (lnC-LA) and CFI and Ismael et al. (2015) found very high positive genetic correlation (0.91) between CFHA (based on activity) and CFI.

Moderate genetic correlations (0.47-0.52) were found between the endocrine fertility traits and 5 to 70 days postpartum milk yield, which is in line with previous studies where undesirable genetic correlations have been found between milk yield and different fertility traits. For example, the genetic correlations of 0.14-0.44 have been
reported between CFI and the milk yield (e.g. Hoekstra et al., 1994; Tenghe et al., 2015). In addition, also unfavorable genetic correlations (0.18-0.45) between milk lnC-LA and milk yield have been reported (Royal et al., 2002; Nyman et al., 2014; Tenghe et al., 2015). For example, Nyman et al. (2014) found a genetic correlation of 0.45 between lnC-LA and 60 days postpartum energy corrected milk yield.

In this study, hyperketonemia traits divided into three classes (ket_s1 and ket_s2) seemed to perform better than bivariate traits in the univariate analysis and were included in the multivariate analysis with endocrine traits and 70 days milk yield. In the current study, genetic correlations between hyperketonemia traits (ket_s1 and ket_s2) and endocrine fertility traits were small, negative and had high standard errors. Instead, genetic correlation between hyperketonemia traits (ket_s1 and ket_s2) and 5 to 70 days milk yield were high, however the standard errors were high as well. In a study by Koeck et al. (2014) moderate genetic correlations (0.13-0.22) were found between EBV of milk BHB and milk yield. Genetic associations found between the milk yield and traits measured from milk BHB concentrations are not surprising as selection for high milk production has negative impacts on cows energy balance and demand a larger fat mobilization in early lactation (e.g. Veerkamp et al., 2003), consequently increasing the risk of hyperketonemia.

Conclusions

Endocrine fertility traits measured from milk progesterone concentration (CFH, C-LA) had higher heritability estimates than traditional fertility traits and the correlation between these traits was very high. Some of the estimates had high standard errors because of the small data size. However, these results suggest that the data on
endocrine fertility traits measured by automatic systems is a promising tool for improving fertility, specifically when more data is available. For hyperketonemia traits, heritability estimates were quite low and there were only slight differences between the different traits studied, however dividing values into three classes instead of two seemed to work somewhat better in the current study. Based on the current study and previous studies, where higher heritabilities have been found for traits based on milk BHB than for clinical ketosis, milk BHB is a promising indicator trait for resistance to ketosis and should be studied more. It is important that this kind of data from automatic devices is made available to recording and breeding organizations in the future.

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Declaration of interest

The authors declare that they have no conflict of interest.

Ethics statement
Herd Navigator™ management program samples and analyses milk progesterone and β-hydroxybutyrate (BHB) automatically during routine milking. No ethics statement is thus required.

Software and data repository resources

No data repository resources are available for this publication.

List of references


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**Table 1** Descriptive statistics for CFH and traditional fertility traits for dairy cows

<table>
<thead>
<tr>
<th>Trait (days)</th>
<th>Parity</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
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</thead>
<tbody>
<tr>
<td>CFI 1</td>
<td>676</td>
<td>78.9</td>
<td>15.8</td>
<td>46.0</td>
<td>184.0</td>
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</tr>
<tr>
<td>CFI 2</td>
<td>625</td>
<td>79.9</td>
<td>17.6</td>
<td>40.0</td>
<td>213.0</td>
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</tr>
<tr>
<td>CFI 3</td>
<td>391</td>
<td>83.5</td>
<td>20.8</td>
<td>51.0</td>
<td>228.0</td>
<td></td>
</tr>
<tr>
<td>CLI 1</td>
<td>676</td>
<td>109.4</td>
<td>43.0</td>
<td>52.0</td>
<td>296.0</td>
<td></td>
</tr>
<tr>
<td>CLI 2</td>
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<td>112.8</td>
<td>40.3</td>
<td>48.0</td>
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<td>46.3</td>
<td>51.0</td>
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<tr>
<td>IFL 1</td>
<td>676</td>
<td>30.5</td>
<td>40.4</td>
<td>0.0</td>
<td>234.0</td>
<td></td>
</tr>
<tr>
<td>IFL 2</td>
<td>625</td>
<td>32.9</td>
<td>43.9</td>
<td>0.0</td>
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<td>IFL 3</td>
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<td>33.5</td>
<td>41.6</td>
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<td></td>
</tr>
<tr>
<td>CFH 1</td>
<td>676</td>
<td>49.9</td>
<td>17.7</td>
<td>22.0</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>CFH 2</td>
<td>625</td>
<td>51.2</td>
<td>17.1</td>
<td>21.0</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>CFH 3</td>
<td>391</td>
<td>53.0</td>
<td>17.2</td>
<td>22.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

CFI = calving to first insemination restricted to ≤230 days; CLI = calving to last insemination restricted to ≤365 days; IFL = interval from first to last insemination; CFH = first heat identified by Herd Navigator restricted to ≤100 days

23
Table 2 Descriptive statistics for CFH, C-LA and milk yield used in multivariate analysis with hyperketonemia traits for first parity cows

<table>
<thead>
<tr>
<th>Trait</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFH, d</td>
<td>763</td>
<td>49.3</td>
<td>17.5</td>
<td>22.0</td>
<td>100.0</td>
</tr>
<tr>
<td>C-LA, d</td>
<td>766</td>
<td>39.8</td>
<td>18.0</td>
<td>21.0</td>
<td>100.0</td>
</tr>
<tr>
<td>milk, kg</td>
<td>670</td>
<td>1774.3</td>
<td>328.3</td>
<td>485.7</td>
<td>2894.4</td>
</tr>
</tbody>
</table>

CFH = first heat identified by Herd Navigator restricted to ≤100 days; C-LA = commencement of luteal activity restricted to ≤100 days; milk = milk yield 5-70 days postpartum
Table 3  Distribution of hyperketonemia values (%) 5 to 60 days postpartum in different classifications of β-hydroxybutyrate values (BHB) and ketosis risk values for first parity cows

<table>
<thead>
<tr>
<th>Trait</th>
<th>negative</th>
<th>suspect</th>
<th>positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>ket_s1&lt;sup&gt;1&lt;/sup&gt;</td>
<td>640(80.6)</td>
<td>86(10.8)</td>
<td>68(8.6)</td>
</tr>
<tr>
<td>ket_s2&lt;sup&gt;2&lt;/sup&gt;</td>
<td>696(87.7)</td>
<td>30(3.8)</td>
<td>68(8.6)</td>
</tr>
<tr>
<td>ket_bin&lt;sup&gt;3&lt;/sup&gt;</td>
<td>726(91.4)</td>
<td></td>
<td>68(8.6)</td>
</tr>
<tr>
<td>ket_r1&lt;sup&gt;4&lt;/sup&gt;</td>
<td>701(88.3)</td>
<td></td>
<td>93(11.7)</td>
</tr>
<tr>
<td>ket_r2&lt;sup&gt;5&lt;/sup&gt;</td>
<td>704(88.7)</td>
<td></td>
<td>90(11.3)</td>
</tr>
</tbody>
</table>

<sup>1</sup> Smoothed BHB values (<0.10, ≥0.10 & <0.20, ≥0.20).
<sup>2</sup> Smoothed BHB values (<0.15, ≥0.15 & < 0.20, ≥0.20).
<sup>3</sup> Smoothed BHB values (<0.20, ≥0.20).
<sup>4</sup> Ketosis risk values (<0.55, ≥0.55).
<sup>5</sup> Ketosis risk values (<0.60, ≥0.60).
Table 4 Heritability estimates ($h^2 \pm$ standard error) from univariate model for traditional fertility traits for first parity cows

<table>
<thead>
<tr>
<th>Trait (days)</th>
<th>$h^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFI</td>
<td>0.07±0.07</td>
</tr>
<tr>
<td>CLI</td>
<td>0.06±0.07</td>
</tr>
<tr>
<td>IFL</td>
<td>0.03±0.06</td>
</tr>
</tbody>
</table>

CFI = calving to first insemination restricted to ≤230 days; CLI = calving to last insemination restricted to ≤365 days; IFL = interval from first to last insemination
Table 5 Heritability estimates ($h^2$± standard error) for CFH, C-LA, milk yield and hyperketonemia traits for first parity cows

<table>
<thead>
<tr>
<th>Trait</th>
<th>$h^2$, multivariate model</th>
<th>$h^2$, univariate model</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFH, d</td>
<td>0.33±0.13</td>
<td>0.19±0.11</td>
</tr>
<tr>
<td>C-LA, d</td>
<td>0.32±0.12</td>
<td>0.24±0.12</td>
</tr>
<tr>
<td>milk, kg</td>
<td>0.30±0.13</td>
<td>0.29±0.13</td>
</tr>
<tr>
<td>ket_s1$^1$</td>
<td>0.10±0.07</td>
<td>0.09±0.07</td>
</tr>
<tr>
<td>ket_s2$^1$</td>
<td>0.08±0.07</td>
<td>0.07±0.07</td>
</tr>
</tbody>
</table>

CFH = first heat identified by Herd Navigator restricted to ≤100 days; C-LA = commencement of luteal activity restricted to ≤100 days; milk = milk yield 5-70 days postpartum; ket_s1 = smoothed BHB values (<0.10, ≥0.10 & <0.20, ≥0.20, restricted 5 to 60 days); ket_s2 = smoothed BHB values (<0.15, ≥0.15 & <0.20, ≥0.20, restricted 5 to 60 days);

$^1$ Either ket_s1 or ket_s2 were included in the multivariate model.
Table 6 Heritability estimates ($h^2 \pm$ standard error) for hyperketonemia traits recorded from 5 to 70 days postpartum for first parity cows from univariate analysis

<table>
<thead>
<tr>
<th>Trait</th>
<th>$h^2$ linear</th>
<th>$h^2$ underlying</th>
<th>$h^2$ logit</th>
<th>$h^2$ probit</th>
</tr>
</thead>
<tbody>
<tr>
<td>ket_s1$^1$</td>
<td>0.09±0.07</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ket_s2$^2$</td>
<td>0.07±0.07</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ket_bin$^3$</td>
<td>0.03±0.06</td>
<td>0.12</td>
<td>0.15</td>
<td>0.07</td>
</tr>
<tr>
<td>ket_r1$^4$</td>
<td>0.05±0.06</td>
<td>0.15</td>
<td>0.14</td>
<td>0.10</td>
</tr>
<tr>
<td>ket_r2$^5$</td>
<td>0.04±0.06</td>
<td>0.12</td>
<td>0.13</td>
<td>0.09</td>
</tr>
</tbody>
</table>

$^1$ Smoothed BHB values (<0.10, ≥0.10 & <0.20, ≥0.20).

$^2$ Smoothed BHB values (<0.15, ≥0.15 & <0.20, ≥0.20).

$^3$ Smoothed BHB values (<0.20, ≥0.20).

$^4$ Ketosis risk values (<0.55, ≥0.55).

$^5$ Ketosis risk values (<0.60, ≥0.60).
Table 7 Genetic (above diagonal) and phenotypic (below diagonal) correlations among CFH, C-LA, milk yield and ket_s1 for first parity cows - Standard errors of estimate in parenthesis

<table>
<thead>
<tr>
<th>Trait</th>
<th>CFH</th>
<th>C-LA</th>
<th>milk</th>
<th>ket_s1</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFH</td>
<td>0.97 (0.02)</td>
<td>0.52 (0.27)</td>
<td>-0.17 (0.42)</td>
<td></td>
</tr>
<tr>
<td>C-LA</td>
<td>0.92</td>
<td>0.47 (0.28)</td>
<td>-0.08 (0.42)</td>
<td></td>
</tr>
<tr>
<td>milk</td>
<td>0.01</td>
<td>0.001</td>
<td>0.59 (0.39)</td>
<td></td>
</tr>
<tr>
<td>ket_s1</td>
<td>0.07</td>
<td>0.06</td>
<td>0.10</td>
<td></td>
</tr>
</tbody>
</table>

CFH = first heat identified by Herd Navigator restricted to ≤100 days; C-LA = commencement of luteal activity restricted to ≤100 days; milk = milk yield 5-70 days postpartum; ket_s1 = smoothed BHB values (<0.10, ≥0.10 & <0.20, ≥0.20, restricted 5 to 60 days)
**Figure captions**

**Figure 1** Milk progesterone curve of a hypothetical dairy cow, used to define endocrine fertility traits. Commencement of luteal activity (C-LA) occurs few days after the first ovulation and the first heat identified by Herd Navigator (CFH) is recorded when the concentration changes from high to low.