## The bovine clinical endometritis and the ratios of serum energy metabolites during the transition period

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#### Abstract

Uterine diseases are common problem that influence the reproductive output in dairy farm. Different factors include metabolic disturbances may affect the uterine defense mechanism and contribute at postpartum uterine disease occurrence. The routine metabolic profile is measurements of net values of non-esterified fatty acids (NEFA),  $\beta$ -hydroxybutyric acid (BHBA), and glucose (Glc) in cow serum. The present study aimed to look at the ratios of the energy metabolic products during the transition period and investigate their relationship with bovine clinical endometritis. The weekly serum samples were collected from 100 dairy cows during the transition period (2 weeks prepartum to 3 weeks postpartum). In the clean test (Day 30 postpartum), 16 cows were selected, and assigned in a case-control repeated measure design into two groups as clinical endometritis (CE: n=8) or healthy cows (n=8). The respective serum samples of the cows were assayed for NEFA, BHBA, and Glc. All the measurement units were converted to mM/L and the ratios were calculated. The trend of changes in the ratios of NEFA to BHBA was in a steady state in healthy cows during the transition period, while it raised at the time of parturition in the CE group (P<0.05). While the significant increase in NEFA to Glc ratio started after parturition in healthy cows, it was begun to increase before parturition in CE. The trend of changes in the energy metabolite ratios during the transition is different in CE compared to healthy dairy cows.

Keywords: Bovine, Clinical endometritis, Energy metabolites, Ratio

#### Introduction

The metabolic disturbance is accompanied by the alterations in three blood metabolic elements; Glucose (Glc), non-esterified fatty acid (NEFA), and  $\beta$ hydroxybutyric acid (BHBA). In common during the transition period, cows experience a low dry matter intake that causes to decrease in the serum Glc. On the other hand, the animal must compensate for its energy requirement through fat mobility from its resources that cause to increase in NEFA. With increased NEFA oxidation, some levels of fatty acids will enter to ketogenesis pathway in the liver (Murray et al., 2009).

The relationship between metabolic disturbances and postpartum uterus diseases

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in dairy cows has been established (Giuliodori et al., 2013a, 2013b; Konyves et al., 2009). All the published studies on the topic, considered the mean net values of metabolic signals, i.e., the serum NEFA, Glc. and BHBA concentrations. in reproductive pathologies of dairy cows. Based on the energy metabolism pathways there are dynamic equations amongst three elements and their changes can be related to each other, i.e., they are converted to each other during energy metabolism. Therefore, the present study aimed to investigate the ratios (NEFA to BHBA, NEFA to Glc, and BHBA to Glc) of the serum energy metabolites (as indicator of their equation) during the transition period in bovine clinical endometritis (CE).

## **Materials and Methods**

The study was conducted in а commercial dairy herd (mean milk yield of 45 kg/day) in the center of Iran (32.3282° N, 50.8769° E) during autumn and winter. The animals were maintained in a free-stall shed and received a diet based on a total mixed ration during the transition period. The blood samples were collected weekly from one hundred selected cows at weeks -2, -1, 0, 1, 2, and 3 of parturition between 0800 to 0100 h, and the collected sera were stored at -80°C until assay. The serum NEFA and BHBA (Randox Laboratories Ltd, UK) and Glc (Pars-Azmoon, Iran) were assayed using specific commercial kits. All of the assays were converted to mM/L to calculate the ratios of NEFA to BHBA (NF/BH), NEFA to Glucose (NF/Glc), and BHBA to Glucose (BH/Glc).

In this case-control repeated measure design, the uterus was examined at day 30 postpartum, using B-mode ultrasound (7.5 MHz) and Fissore, Edmondson, Pashen, and Bondurant (1986) indices for defining CE; accumulation of non-echogenic fluid containing snowy particles within uterus with thickened uterine wall. The animals with dystocia, the retained placenta, or metritis in the respected parturition were excluded. Sixteen cows were selected and equally assigned into two groups as CE and healthy. Their respective collected serum samples were subjected to assay.

Two-way repeated-measures ANOVA with pdiff post hoc test was used for data analysis in SAS (SAS/stat 9.2 user guide). The data were expressed as the Least square means and standard error of the mean. P<0.05 was considered significant.

## Results

Nineteen cows were diagnosed as clinical endometritis in the study that 12 cows were had no history of dystocia, retained fetal membrane, ketosis or milk fever.

Figure 1 shows that the serum NEFA begins to increase from a week of precalving in endometritis cows, while changes are significant from the time of calving onwards in healthy cows. The serum BHBA and Glc changes were not significantly different during the period of the study between the two groups.

NF/BH at the calving week was higher than other weeks in the CE group (Figure 2; P<0.05). The weekly comparison showed lower levels of NF/BH in the healthy  $(0.73\pm0.64)$  compared to CE groups  $(2.3\pm0.36; P=0.03)$ . NF/Glc was mainly under influence of weeks rather than endometritis. NF/Glc at calving week was the highest among all the weeks in the CE group (P<0.05). NF/Glc increased during the post-calving weeks (weeks 1 and 2) in the healthy group (P<0.05). Figure 2 shows no change in BH/Glc either in terms of the main effects or interaction of the weeks and groups (P>0.05).

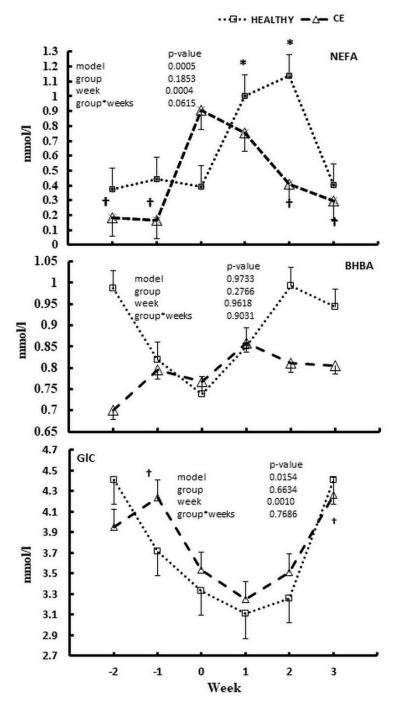


Figure 1. The serum energy metabolites (LSmean±SEM) in healthy (n=8) and CE (n=8) dairy cows during the transition period (wk 0= week of calving). \* indicates a significant difference compared to wk 0 within the healthy group (P<0.05). †indicates significant difference compared to wk 0 within the CE group (P<0.05). CE: clinical endometritis; NEFA: non-esterified fatty acid; BHBA:  $\beta$ -hydroxybutyric acid and Glucose: Glc.

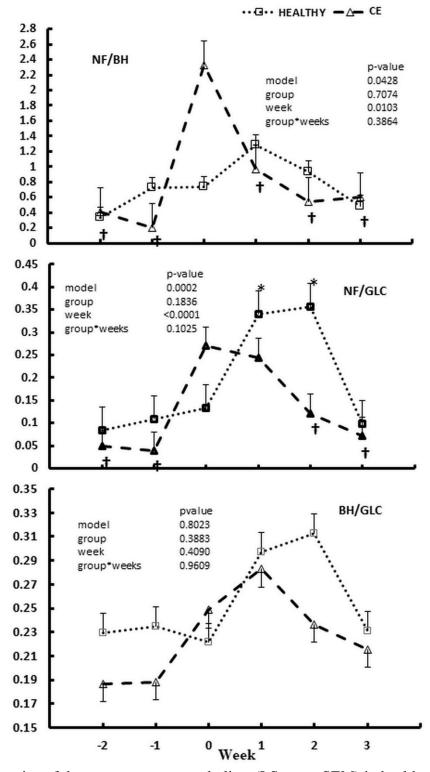


Figure 2. The ratios of the serum energy metabolites (LSmean±SEM) in healthy (n=8) and CE (n=8) dairy cows during the transition period (wk 0= week of calving). \* indicates a significant difference compared to wk 0 within the healthy group (P<0.05). †indicates significant difference compared to wk 0 within the CE group (P<0.05). CE: clinical endometritis; NF: non-esterified fatty acid; BH:  $\beta$ -hydroxybutyric acid and Glucose: Glc.

### Discussion

In the current study, we observed altered prepartum early serum NEFA concentrations in CE compared to healthy cows. The changes of the serum BHBA and Glc were not so different in both groups of animals. The weekly patterns of NF/BH and NF/Glc were considerable in the cases of the bovine CE. The healthy cows showed changes after calving with a steady-state pattern before calving. The animals in the CE group had started the changes from two weeks of pre-calving. BH/Glc was not different between groups during all the sampling time points. It has been established that by reducing food intake during the prepartum period, the animals change their source of energy from Glc to NEFA. The free fatty acid mobilization and metabolism accelerate the ketone body production; i.e., acetoacetate, acetone, and BHBA. In the present study, the CE cows showed an early pre-calving transition to the NEFA production with decreasing the associated serum Glc that was recovered during early postpartum by reducing NEFA and rising Glc. However, NF/Glc in the healthy animals was started to increase after parturition and continued for a longer time. Since the stress, as well as negative energy balance, may increase the NEFA (Murray et al., 2009), the causes of discrepant NEFA can be different in the groups. Based on the modifications in serum Glc and NEFA, it looks that changes in the ratio in the healthy cows can be a stress-induced phenomenon. As the serum BHBA followed a steady-state condition in both groups, it assumes that NF/BH was mainly related to the NEFA concentrations. The trends of changes of BH/Glc in both groups were also similar to NF/Glc. By rising the serum Glc from week 1, the ratio started to decrease in CE cows and continued rising in the healthy animals, which may relate to the stress or the negative energy balance. The serum Glc concentrations may rise following increased dry matter intake or some stressful conditions.

The disturbances in the uterine immune defense system have been also considered in subclinical ketosis (Hammon, Evjen, Dhiman, Goff, & Walters, 2006). Alteration in the uterine immune system can cause uterine infections in cases with higher BHBA and NEFA. It was shown that longhyperketonemia term would be accompanied by metritis via reducing insulin (Kerestes et al., 2009) or reducing activities of IGF-I. Bicalho, Marques, Gilbert, and Bicalho (2017) showed higher concentrations of plasma Glc in the CE cows compared to the healthy cows with no effect of BHBA and NEFA, which are in contrast to the present findings. Reduced interferon  $\gamma$  in the peripheral blood monocytes from cows due to NEFA (Ster, Loiselle, & Lacasse, 2012) and a reduced influx of immune cells to the mammary gland due to higher plasma BHBA levels Wellnitz. Dorland. (Zarrin. van & Bruckmaier, 2014) are indicators of the immunosuppression following the metabolic disturbances in dairy cows. The results of this study may address the possible potentials of the pre-calving ratios of the energy metabolites (NF/BH and NF/Glc) for predicting the risk for CE in dairy cows.

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## **Conflict of interest**

The authors declare no conflict of interest.

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# متابولیتهای انرژی در طول فاز انتقالی و اندومتریت بالینی در گاوشیری

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چکیدہ

بیماریهای رحم مشکل شایع هستند که بر عملکرد تولید مثل در دامداریهای گاو شیری تأثیر میگذارد. عوامل مختلف از جمله اختلالات متابولیک ممکن است بر مکانیسم دفاعی رحم تأثیر بگذارد و در بروز بیماری رحم پس از زایمان نقش داشته باشند. شاخصهای معمول متابولیک شامل اندازهگیری مقدار خالص اسیدهای چرب غیر استریفیه (NEFA)، - (هیدروکسی بوتیریک اسید (BHBA) و گلوکز Ord در سرم گاو هستند. مطالعهی حاضر با هدف بررسی نسبت محصولات حاصل از متابولیسم انرژی در طول دوره گذار و بررسی ارتباط آنها با اندومتریت بالینی گاو انجام شده است. نمونههای سرمی هفتگی از ۱۰۰ گاو شیری در طول دوره انتقال (۲ هفته قبل از زایمان تا ۳ هفته پس از زایمان) جمع آوری شد. در معاینهی روز ۳۰ پس از زایمان، ۱۶ گاو شیری در طول دوره انتقال (۲ هفته قبل از زایمان تا ۳ هفته پس از زایمان) جمع آوری شد. در معاینهی روز ۳۰ پس از زایمان، ۱۶ گاو انتخاب شدند و در قالب طرح آزمایشی با اندازهگیری مکرر به صورت موردی به دو گروه به عنوان اندومتریت بالینی (E : n علی اندازهگیری سالم (8 = n) تقسیم شدند. نمونه مرم مربوط به گاوها برای NEFA، ABHB و GD مورد سنجش قرار گرفت. همهی واحدهای اندازهگیری به LMM تبدیل و نسبتها محاسبه شد. روند تغییرات نسبتهای ABHA به BHBA در گاوهای سالم در طول دوره گذار در حالت اسبتها مروع شد، و در زمان زایمان در گروه CE افزایش یافت. در حالی که افزایش قابل توجه نسبت ABH به GD پس از زایمان در گاوهای سالم شروع شد، زایمان در گروه CE افزایش یافت. در حالی که افزایش قابل توجه نسبت ABH به GL پس از زایمان در گاوهای سالم شروع شد، زمان زایمان در گروه CE افزایش یافت. در حالی که افزایش قابل توجه نسبت ABH به GL پس از زایمان در گاوهای سالم شروع شد، زایمان در گروه CE افزایش یافت. در حالی که افزایش قابل توجه نسبت متابولیت انرژی در طول انتقال در CE در مقایسه با گاوهای سالم شروع شد، تر مان در مان در مان در مان مدر مروه کا فزایش یلی در حال مدر طول در زمان در گروه CE افزایش یافت. در حالی که افزایش قابل توجه نسبت می به به کاو مای در گاوهای سالم شروع شد، مران در گروی می می فزایش در حالی که فزایش قابل توجه نسبت می به می می در طول انتقال در CE در مقایسه با گاوهای سالم شروع شد، مران در خان در خان در می مان در مان در مول انتقال در حام در مولی در می در می مای در مان در می می می به می می در می در می می

**کلمات کلیدی**: گاو شیری، متابولیتهای انرژی، نسبت، آندومتریت بالینی

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