

LIVER HEALTH IN THE PERIPARTURIENT PERIOD AND ITS EFFECT ON MILK PRODUCTION AND REPRODUCTION IN DAIRY COWS

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ABSTRACT

The periparturient period is a critical phase in dairy cows because negative energy balance and lipid mobilization may impair liver function, milk production, and reproductive performance. The aim of this study was to evaluate the relationship between energy balance, liver health indicators, milk production, and pregnancy success after the first insemination in multiparous dairy cows from a commercial herd with high milk production. Forty cows were assessed using production records, reproductive data, biochemical blood parameters, and calculated liver indices, including the liver functionality index (LFI) and liver health index (LHI). The results indicate that cows with more favorable liver health indicators showed better metabolic adaptation after calving and more favorable production and reproductive outcomes. The findings support the practical use of LHI as a simple tool for early identification of cows at risk of impaired transition performance.

Keywords: liver, energy balance, milk production, reproduction

INTRODUCTION

The periparturient period, approximately 21 days before and 21 days after calving, represents a phase of substantial physiological and metabolic changes in dairy cows. This metabolic challenge is associated with the high energy requirements for fetal growth in late gestation and preparation of the mammary gland for the subsequent lactation (Haitao et al. 2025). The early postpartum period is particularly critical because feed intake is often insufficient to meet the energy demands associated with tissue recovery and onset of lactation. This results in negative energy balance (NEB) and increased lipomobilization (Wathes et al. 2007; LeBlanc 2012). Reduced feed intake decreases ruminal propionic acid production, an important precursor for glucose synthesis (Weber et al. 2013).



To compensate for the energy deficit, dairy cows mobilize adipose tissue through lipolysis, releasing non-esterified fatty acids (NEFA) into the bloodstream. These fatty acids are subsequently metabolized in the liver (Mao et al. 2026). When circulating NEFA concentrations are high, hepatic metabolic capacity may be exceeded, resulting in lipid accumulation in the liver and contributing to fatty liver development (White 2015; Haitao et al. 2025). Disruption of metabolic processes during the periparturient period increases the risk of metabolic disorders, particularly ketosis, which negatively affects milk production. In addition, secondary reproductive health problems may occur, including retained placenta, bacterial uterine infections, and impaired estrous cyclicity (Abdelli et al. 2017).

The first 21 days after calving are also influenced by inflammatory conditions associated with increased cytokine production as a consequence of lipid mobilization (Contreras, Sordillo 2011). During this phase, cytokines contribute to the redistribution of nutrients among tissues and organs according to current physiological priorities and also affect dry matter intake (DMI) and reproductive performance in dairy cows (Montagner et al. 2016). In the liver, cytokines are involved in inflammatory responses, increasing the concentrations of positive acute-phase proteins and decreasing negative acute-phase proteins, including albumin (Bionaz et al. 2007).

In high-producing dairy cows, proper liver function is essential for maintaining high milk yield and minimizing health disorders. The liver is one of the most important metabolic organs because it is responsible for key processes such as gluconeogenesis, fatty acid metabolism, and protein synthesis, while also playing an important role in immune regulation (Drackley 2025). A healthy and functional liver is therefore a prerequisite for sufficient gluconeogenesis and the synthesis of metabolites required for milk production in the mammary gland. Impaired liver function during the periparturient period is often associated with reduced milk yield and shorter lactation length (Weber et al. 2013).

One approach to evaluating the extent of inflammatory processes and liver functionality is the liver functionality index (LFI), which considers changes in serum concentrations of bilirubin, albumin, and cholesterol in dairy cows on days 3 and 28 after calving (Zhou et al. 2016). LFI can be used to assess the success of adaptation to early lactation. However, a limitation of this indicator is the need for repeated sampling at precisely defined time intervals (Kerwin et al. 2022). LFI enables assessment of the extent of the inflammatory response and prediction of its potential impact on animal health (Bertoni and Trevisi 2013). In intensive systems, cows with low LFI have been shown to have lower dry matter intake, reduced milk production, and a higher incidence of disease (Trevisi et al. 2012). However, it has not been clearly demonstrated whether similar results occur in semi-extensive systems, where environmental factors such as heat stress must also be considered (Montagner et al. 2016).

Another approach to assessing hepatic load is the liver health index (LHI), which is based on a single blood sample collected 3–12 days after calving. This method

may help farmers identify cows at risk of impaired adaptation to lactation at an early stage. LHI uses serum concentrations of bilirubin, cholesterol, and albumin, which are individually compared with the values of other cows in the herd using the mean and standard deviation. Cows with higher LHI values have been reported to have higher milk yield, more days in milk (DIM), and lower NEFA concentrations (Kerwin et al. 2022; Nelson et al. 2024).

The aim of this study was to evaluate the relationship between energy balance, liver function, milk production, and pregnancy success after first insemination in dairy cows under farm conditions with an average milk production above 9,000 kg. The underlying hypothesis was that impaired energy balance and reduced liver function during the periparturient period negatively affect productive and reproductive indicators in dairy cows.

MATERIALS AND METHODS

The evaluation was carried out on a selected dairy farm with a controlled nutritional management system and an average annual milk production of 8,000–10,000 kg per cow. Cows were housed in a freestall barn in a separate group and fed a total mixed ration (TMR) formulated according to NRC (2001) recommendations for different phases of the production cycle in multiparous dairy cows. Multiparous dairy cows ($n = 40$) were evaluated for nitrogen utilization efficiency and energy balance in relation to pregnancy success after first insemination. Samples of the TMR were collected from the feed manger on the control day and analyzed for dry matter (DM), crude protein (CP), acid detergent fiber (ADF), neutral detergent fiber (NDF), starch, and ether extract (EE) using conventional methods according to Commission Regulation (EC) No. 691/2013. Net energy for lactation (NEL) and non-fibrous carbohydrate (NFC) values were calculated using regression equations according to NRC (2001).

All cows were enrolled in a Presynch Ovsynch protocol. Controlled reproduction was applied from the 70th day after parturition. The success of reproduction was evaluated in dairy cows by transrectal ultrasonography of the ovaries and uterus.

Analysis of production parameters was performed on the control day using individually collected milk samples. Milk yield, milk components, and milk urea were evaluated. Total protein, fat, lactose, and urea concentrations were analyzed by near-infrared spectrophotometry using MilkoScan FT⁺ and BENTLEY FTS at the Central Analytical Laboratory of Milk, accredited under registration number 096/5878/2015/2.

Energy balance was evaluated as the difference between the actual energy intake from the TMR and the energy output in milk nutrients, expressed as positive or negative NEL balance in MJ/day and calculated according to Daniel et al. (2017).

Efficiency of nitrogen utilization (EUN) was estimated for the group of dairy cows based on the analyzed MUN content and milk yield using the regression equation developed by Huhtanen et al. (2015) from meta-analytical assessments of balance experiments.

Statistical analyses were performed using GraphPad Prism 9. Each parameter was presented as its mean (x), and standard deviation (SD).

Blood samples for biochemical analysis were collected at regular intervals: 7 days before the expected calving date, 7 days after calving, 20 days after calving, and 60 days after calving. Samples were collected from the coccygeal vein in the morning after feeding and immediately transported to the laboratory for processing.

Metabolites of intermediary metabolism were determined photometrically using diagnostic kits and an Ellipse biochemical analyzer (Spain). The assessment included markers of energy metabolism (CHOL, cholesterol; TG, triacylglycerol; NEFA, non-esterified fatty acids; BHBA, beta-hydroxybutyric acid), protein metabolism (TP, total protein; ALB, albumin; urea), and liver load (BIL, bilirubin; AST; GGT).

To assess hepatic load, LHI was calculated using samples collected 7–10 days after calving. Serum concentrations of bilirubin, cholesterol, and albumin were determined in the laboratory and subsequently used in the LHI calculation according to Kerwin et al. (2022).

Milk performance and reproductive records were obtained from the software program used on the evaluated farm and from the Breeding Services of the Slovak Republic (PLIS).

RESULTS AND DISCUSSION

Evaluation of nutritional composition

The average nutrient concentrations in the TMR used on the evaluated farm are presented in Table 1. The feed ration, based on corn and ryegrass silages with the addition of concentrate feed, was formulated for multiparous dairy cows with a target milk production of 45 kg/day, 3.3 % milk protein, and 3.6 % milk fat.

Evaluation of milk production, energy balance, nitrogen utilization, and reproduction

The evaluation of milk production, energy balance, and the efficiency of nitrogen utilization according to days in milk is summarized in Table 2. Analysis of energy balance, assessed on the basis of energy intake in the diet and nutrient output in milk according to Daniel et al. (2017), confirmed different levels of negative energy balance in the evaluated cows. The mean energy balance ranged from -43.4 MJ/day shortly after calving to -3.5 MJ/day at peak lactation. Negative energy balance reflects the degree of lipid mobilization and, at the beginning of lactation, corresponds to the energy requirements for the synthesis of approximately 14 kg of milk.

These findings indicate that the extent of postpartum negative energy balance represents an important biological mechanism linking metabolic load, liver function, and subsequent reproductive success in dairy cows.

Tab. 1: Nutritional composition of the total mixed ration (TMR)

	Antepartum	Postpartum	Early lactation
	X ± SD	X ± SD	X ± SD
DM g	346.9 ± 65.0	426.3 ± 39.7	412.7 ± 9.3
CP g/kg DM	153.3 ± 12.1	164.9 ± 12.4	164.8 ± 16.6
PDIN	99.4 ± 6.6	113.3 ± 9.5	112.8 ± 12.4
PDIE	87.0 ± 10.6	111.3 ± 9.8	109.3 ± 8.9
NDF g/kg DM	425.8 ± 42.5	327.3 ± 19.6	330.2 ± 10.2
ADF g/kg DM	275.1 ± 32.5	192.8 ± 10.9	195.7 ± 9.3
Starch g/kg DM	172.9 ± 46.3	271.7 ± 24.7	280.9 ± 31.5
EE g/kg DM	30.7 ± 4.0	33.5 ± 5.9	32.3 ± 2.8
Ash g/kg DM	74.0 ± 7.8	66.3 ± 4.9	69.0 ± 3.5
NEL MJ/kg DM	5.89 ± 0.5	6.99 ± 0.3	7.00 ± 0.15
DMI kg	19.3 ± 0.7	20.5 ± 0.8	23.6 ± 0.9
NEL intake MJ/d	113.7	143.3	165.2

Composition: corn silage 26 – 30 kg, ryegrass silage 10 kg, GPS silage 9 kg, wheat straw 0.5 – 0.8 kg, corn cob mix (CCM) 5.0 – 7.5 kg, dried distillers grains (DDG) 3.5 kg, rapeseed meal 4.0 – 4.3 kg, CornGold 2.0 – 2.5 kg, molasses 0.5 kg, and feed mixture 1.8 – 2.2 kg.

DM = dry matter; DMI = dry matter intake.

Tab. 2: Milk production, energy balance, and efficiency of nitrogen utilization

	<25 DIM	25 – 60 DIM	60 – 90 DIM
Milk production, kg/day	33.85 ± 6.3	44.60 ± 12.1	43.40 ± 12.3
Milk fat, %	4.75 ± 1.29	3.39 ± 1.65	2.95 ± 1.03
Total yield, kg	1.42 ± 0.6	1.38 ± 0.6	1.24 ± 0.5
Milk protein, %	3.41 ± 0.35	3.18 ± 0.34	3.31 ± 0.18
Total yield, kg	1.05 ± 0.4	1.39 ± 0.3	1.43 ± 0.4
Fat-to-protein ratio	1.39 ± 0.36	1.04 ± 0.39	0.89 ± 0.31
Lactose, %	4.81 ± 0.18	4.79 ± 0.33	4.77 ± 0.25
Energy balance MJ NEL/day	-43.4 ± 38.8	- 31.2 ± 35.4	- 3.5 ± 31.5
EUN %	29.2 ± 4.9	31.7 ± 4.1	31.9 ± 2.43
Milk urea, mg/dL	24.43 ± 10.66	25.17 ± 10.98	21.93 ± 7.02
MUN, mg/dL	11.48 ± 5.04	11.83 ± 5.16	10.31 ± 3.30

In the evaluated cows, the highest mean milk production was recorded during the first phase of lactation, reaching 43.40 ± 12.3 kg/day. Increased milk production may reduce fertility, particularly as a consequence of inadequate transition-period management, different levels of postpartum NEB, or a higher incidence of disease. The extent and duration of NEB are closely related to dry matter intake. NEB accompanied by lipid mobilization affects the physiological mechanisms of the reproductive endocrine cascade. At the beginning of lactation, milk synthesis

is associated with increased growth hormone concentrations, which redistribute nutrients mainly in the liver and adipose tissue (Lucy, 2008). As a consequence of NEB, insulin concentrations remain low, preventing the increase in hepatic growth hormone receptors and IGF-I secretion, thereby negatively affecting reproduction. Insulin and IGF-I are then unable to act synergistically with gonadotropins on ovarian cells, which may prevent ovulation of the dominant follicle (Butler 2005) and delay the resumption of cyclicity (Wathes 2007). Increased milk production is also negatively correlated with the intensity of estrus expression (Madureira et al. 2015) or with reduced locomotor activity (Yániz et al. 2006).

Evaluation of liver health and liver function

Concentrations of intermediary metabolism metabolites in dairy cows during the evaluated period from 7 to 60 days in milk are shown in Table 3. Mean concentrations of cholesterol, bilirubin, and AST increased between sampling points compared with the other evaluated metabolites. The concentrations and trends of intermediary metabolism metabolites corresponded with physiological changes after calving and during early lactation. At the level of intermediary metabolism, the degree of NEB is assessed mainly through the concentration of non-esterified fatty acids (NEFA). In the present evaluation, serum NEFA concentrations did not differ markedly among cows and averaged 0.25–0.28 mmol/L.

Tab. 3: *Metabolites of intermediary metabolism in dairy cows from 7 to 60 days in milk*

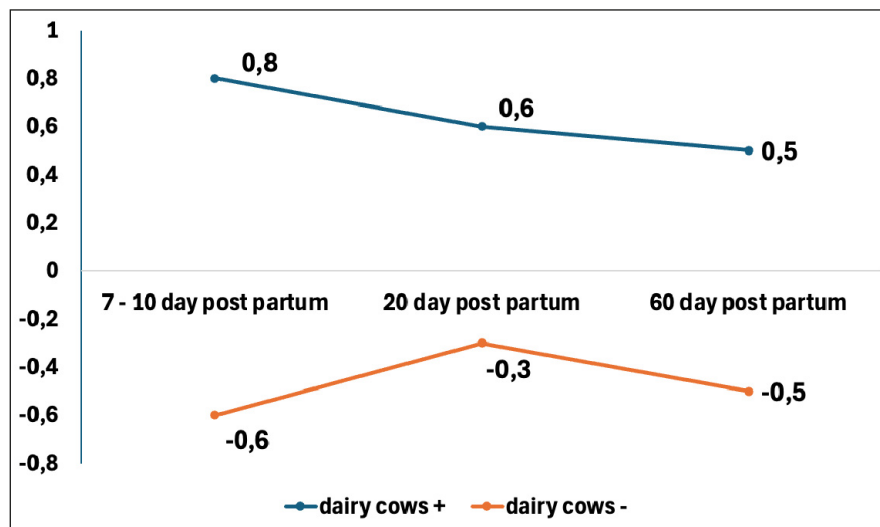
	7–10 days postpartum	20 days postpartum	60 days postpartum
TP g/l	71.91 ± 6.31	78.83 ± 4.88	73.07 ± 6.74
ALB g/l	33.65 ± 3.43	33.65 ± 3.30	33.92 ± 3.15
UREA mmol/l	4.25 ± 0.91	4.20 ± 1.05	4.98 ± 1.24
CHOL mmol/l	2.07 ± 0.66	2.60 ± 0.89	4.44 ± 1.60
TG mmol/l	1.01 ± 0.13	0.98 ± 0.08	1.00 ± 0.08
NEFA mmol/l	0.28 ± 0.17	0.25 ± 0.11	0.26 ± 0.15
BHBA mmol/l	0.76 ± 0.32	0.73 ± 0.32	0.80 ± 0.30
BIL mmol/l	3.17 ± 1.19	4.24 ± 2.85	6.64 ± 5.26
GGT µkat/l	0.45 ± 0.20	0.45 ± 0.13	0.54 ± 0.18
AST µkat/l	1.38 ± 0.29	1.42 ± 0.30	1.54 ± 0.38

Peak lactation is characterized by NEB, higher blood NEFA concentrations, and the most pronounced increase in milk production (Drackley, 1999). Postpartum increases in NEFA concentration and decreases in glucose concentration are negatively correlated with pregnancy success at first insemination in artificial insemination programs (Garverick et al. 2013). BHBA concentrations can be used as a marker of NEB, and increased BHBA values associated with hyperketonemia negatively affect milk production, culling rate, and reproductive performance (McArt et al. 2012). McArt et al. (2012) confirmed that cows with subclinical ketosis

between days 3 and 7 after calving were less likely to become pregnant after first service during the first 30 days postpartum than cows in which ketosis developed on day 8 or later.

According to Ospina et al. (2010) and McArt et al. (2013), elevated serum concentrations of BHBA and NEFA in dairy cows during the periparturient period represent a risk factor for the success of the first postpartum insemination. Under these conditions, both the immune and endocrine systems are involved in adaptation. The resulting metabolic load may impair reproductive performance and reduce milk production, which are key indicators of profitability in dairy farms (Esposito et al. 2014).

The liver functionality index (LFI) was calculated according to Bertoni and Trevisi (2013) from albumin, cholesterol, and bilirubin concentrations measured 7 or 10 days and 20 days after calving. In the positive group of cows (+), the LFI value was -0.55, which was higher than in the negative group of cows (-), where LFI reached -3.54. Mezzetti et al. (2021) reported that cows with the lowest LFI values had the lowest milk yield, the poorest reproductive parameters, and the highest incidence of disease at the beginning of lactation. Therefore, LFI calculation represents a useful tool for monitoring the adaptation of dairy cows to the postpartum period and early lactation.



Graph 1: Liver health index in dairy cow

The liver health index (LHI) was subsequently determined in selected cows and is shown in Graph 1 for both evaluated groups (+ and -). In the positive group of cows (+), LHI ranged from 0.5 to 0.8, whereas in the negative group (-), it reached negative values ranging from -0.6 to -0.3. Kerwin et al. (2022) reported that cows with higher LHI had a lower incidence of reproductive disorders after calving, higher milk yield, and better pregnancy success than cows with lower LHI values. LHI assessment can therefore be considered an economically and practically advantageous monitoring method under farm conditions, as it requires only one blood sample shortly after calving.

Available studies indicate that severe negative energy balance during the periparturient period and an increased incidence of metabolic disorders are associated with impaired liver function. Low LHI values are usually related to increased concentrations of NEFA and BHBA, which negatively affect subsequent reproductive performance and the overall health status of dairy cows in the herd (Ospina et al. 2010; Kerwin et al. 2022).

CONCLUSION

Both LHI and LFI use serum concentrations of bilirubin, albumin, and cholesterol to evaluate the functional status of the liver. LFI assesses the dynamics of these indicators between repeated sampling points after calving, whereas LHI provides a practical assessment of liver health based on a single sample collected during the early postpartum period. From the perspective of routine herd monitoring, LHI is therefore a more suitable tool for the early identification of at-risk cows and for supporting decisions regarding nutritional and veterinary interventions (Zhou et al. 2016; Kerwin et al. 2022).

Assessment of liver health using LHI may help identify at-risk animals shortly after calving without the need for repeated testing later in lactation. Early diagnosis may therefore contribute to more targeted management of negative energy balance, reduction of metabolic risks, and improvement of both productive and reproductive efficiency in the herd.

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REFERENCES

- ABDELLI, Amine, et al. Elevated non-esterified fatty acid and β -hydroxybutyrate in transition dairy cows and their association with reproductive performance and disorders: A meta-analysis. *Theriogenology*, 2017, 93: 99–104.
- BERTONI, Giuseppe; TREVISI, Erminio. Use of the liver activity index and other metabolic variables in the assessment of metabolic health in dairy herds. *Veterinary Clinics: Food Animal Practice*, 2013, 29.2: 413–431.
- BIONAZ, M. et al. Plasma paraoxonase, health, inflammatory conditions, and liver function in transition dairy cows. *Journal of dairy science*, 2007, 90.4: 1740–1750.
- BUTLER, W. R. Nutrition, negative energy balance and fertility in the postpartum dairy cow. *Cattle Pract*, 2005, 13.1: 13–8.
- CONTRERAS, G. Andres; SORDILLO, Lorraine M. Lipid mobilization and inflammatory responses during the transition period of dairy cows. *Comparative Immunology, Microbiology and Infectious Diseases*, 2011, 34.3: 281–289.

- DANIEL, Jean-Baptiste, et al. A method to estimate cow potential and subsequent responses to energy and protein supply according to stage of lactation. *Journal of dairy science*, 2017, 100.5: 3641–3657.
- DRACKLEY, James K. Biology of dairy cows during the transition period: The final frontier?. *Journal of dairy science*, 1999, 82.11: 2259–2273.
- DRACKLEY, James K. Dietary Interventions for Optimal Liver Function in High-Yielding Dairy Cows. *Annual Review of Animal Biosciences*, 2025, 14.
- ESPOSITO, Giulia, et al. Interactions between negative energy balance, metabolic diseases, uterine health and immune response in transition dairy cows. *Animal reproduction science*, 2014, 144.3-4: 60–71.
- GARVERICK, H. A., et al. Concentrations of nonesterified fatty acids and glucose in blood of periparturient dairy cows are indicative of pregnancy success at first insemination. *Journal of dairy science*, 2013, 96.1: 181–188.
- HU, Haitao, et al. An overview of the development of perinatal stress-induced fatty liver and therapeutic options in dairy cows. *Stress Biology*, 2025, 5.1: 14.
- HUHTANEN, Pekka, et al. Evaluation of between-cow variation in milk urea and rumen ammonia nitrogen concentrations and the association with nitrogen utilization and diet digestibility in lactating cows. *Journal of Dairy Science*, 2015, 98.5: 3182–3196.
- KERWIN, A. L., et al. Associations of a liver health index with health, milk yield, and reproductive performance in dairy herds in the northeastern United States. *JDS communications*, 2022, 3.6: 446–450.
- LEBLANC, S. J. Interactions of metabolism, inflammation, and reproductive tract health in the postpartum period in dairy cattle. *Reproduction in Domestic Animals*, 2012, 47: 18–30.
- LUCY, MC. Functional differences in the growth hormone and insulin-like growth factor axis in cattle and pigs: implications for post-partum nutrition and reproduction. *Reproduction in Domestic Animals*, 2008, 43: 31–39.
- MADUREIRA, A. M. L., et al. Factors affecting expression of estrus measured by activity monitors and conception risk of lactating dairy cows. *Journal of Dairy Science*, 2015, 98.10: 7003–7014.
- MAO, Siqing, et al. Hepatotoxicity of Nonesterified Fatty Acids to Dairy Cows: Pathophysiological Mechanisms and Prospective Solutions. *Animal Research and One Health*, 2026, 4.2: 167–184.
- MCART, Jessica AA, et al. Elevated non-esterified fatty acids and β -hydroxybutyrate and their association with transition dairy cow performance. *The Veterinary Journal*, 2013, 198.3: 560–570.
- MEZZETTI, Matteo, et al. The transition period updated: A review of the new insights into the adaptation of dairy cows to the new lactation. *Dairy*, 2021, 2.4: 617–636.
- MONTAGNER, Paula, et al. Reduction of liver function delays resumption of post-partum ovarian activity and alters the synthesis of acute phase proteins in dairy cows. *Research in Veterinary Science*, 2016, 106: 84–88.

- MONTAGNER, Paula, et al. Relationship between pre-partum body condition score changes, acute phase proteins and energy metabolism markers during the peripartum period in dairy cows. *Italian Journal of Animal Science*, 2017, 16.2: 329–336.
- NATIONAL RESEARCH COUNCIL, 2001. *Nutrient Requirements of Dairy Cattle*. 7th rev. ed. Washington, DC: National Academy Sciences. ISBN 978-0-309-06997-7.
- NELSON, Tate Michael, 2024. *Nutritional Factors That Influence Rumen and Liver Health During the Periparturient Period*. Ithaca, NY. PhD thesis. Cornell University.
- OSPINA, P. A., et al. Associations of elevated nonesterified fatty acids and β -hydroxybutyrate concentrations with early lactation reproductive performance and milk production in transition dairy cattle in the northeastern United States. *Journal of dairy science*, 2010, 93.4: 1596–1603.
- TREVISI, ERMINIO, et al. Metabolic stress and inflammatory response in high-yielding, periparturient dairy cows. *Research in veterinary science*, 2012, 93.2: 695–704.
- WATHES, D. C., et al. Differences between primiparous and multiparous dairy cows in the inter-relationships between metabolic traits, milk yield and body condition score in the periparturient period. *Domestic animal endocrinology*, 2007, 33.2: 203–225.
- WEBER, C., et al. Hepatic gene expression involved in glucose and lipid metabolism in transition cows: Effects of fat mobilization during early lactation in relation to milk performance and metabolic changes. *Journal of dairy science*, 2013, 96.9: 5670–5681.
- WHITE, Heather M. The role of TCA cycle anaplerosis in ketosis and fatty liver in periparturient dairy cows. *Animals*, 2015, 5.3: 793–802.
- YÁNIZ, J. L., et al. Factors affecting walking activity at estrus during postpartum period and subsequent fertility in dairy cows. *Theriogenology*, 2006, 66.8: 1943–1950.
- ZHOU, Z., et al. Circulating amino acids in blood plasma during the peripartal period in dairy cows with different liver functionality index. *Journal of dairy science*, 2016, 99.3: 2257–2267.