



Effect of Calf Delivery Mode on Irisin, Asprosin, Leptin, Adiponectin, and Insulin-Like Growth Factor-1 Levels in Dairy Cattle and their Calves

Meltem Kızıl^{1*}, Ali Rişvanlı², Murat Abay³, Tarık Şafak⁴, Mehmet Akif Kılıncı⁵, Öznur Yılmaz⁶, Burak Fatih Yüksel¹ and İbrahim Şeker¹

¹Department of Phisiology, Faculty of Veterinary Medicine, Firat University, Elazig, Turkey.

²Department of Obstetrics and Gynecology, Faculty of Veterinary Medicine, Kyrgyz-Turkish Manas University, Bishkek, Kyrgyzstan.

³Department of Obstetrics and Gynecology, Faculty of Veterinary Medicine, Erciyes University, Kayseri, Turkey.

⁴Department of Obstetrics and Gynecology, Faculty of Veterinary Medicine, Kastamonu University, Kastamonu, Turkey.

⁵Department of Obstetrics and Gynecology, Faculty of Veterinary Medicine, Bingöl University, Bingöl, Turkey.

⁶Department of Obstetrics and Gynecology, Faculty of Veterinary Medicine, Siirt University, Siirt, Turkey.

ABSTRACT

In recent years, the investigation of peptide and protein-structured hormones in biological fluids has become one of the most striking issues. The aim of this study was to determine irisin, asprosin, leptin, adiponectin, and IGF-1 levels in cows and calves after calving according to the mode of delivery. The study was carried out with 20 Holstein cows and 20 calves born from these cows. Blood samples were taken from cows and calves in all groups during birth, after drinking colostrum from calves and on the 15th, 30th, 45th and 60th days after birth in 10 ml tubes. The levels of the aforementioned molecules in these blood samples were determined by ELISA method. Feeding with colostrum led to a decrease in the irisin levels in the dystocia and cesarean section groups and in the IGF-1 levels in the vaginal delivery group, but it did not lead to any other significant changes. The irisin levels of the calves in the vaginal delivery group were compared to those in the other groups, and their levels were found to decrease on the 15th day, and IGF-1 levels were higher on the 15th day. As a result, it was revealed that there were significant changes in the levels of these molecules in the umbilical cord and blood serum of cows and calves depending on the mode of delivery.

INTRODUCTION

The largest source of energy in an organism is adipose tissue, and it is known that adipose tissue does not merely act as energy storage, but also works as an endocrine organ by synthesizing various cytokines and


hormones (Ahima and Flier, 2000). Adipose tissue synthesizes and secretes many different molecules, such as irisin, asprosin, leptin, and adiponectin (Dua *et al.*, 1996).

Irisin is a thermogenic protein that was discovered in 2012. It facilitates energy consumption by converting white adipose tissue to brown adipose tissue. The main physiological role of irisin is to pass into white adipose tissue from circulation and convert it to brown adipose tissue, resulting in fat breakdown (Boström *et al.*, 2012). Although it had been known that brown adipose tissue contributes to the regulation of body temperature in infants (Lidell and Enerbäck, 2010), its function in adult physiology remained unknown until the irisin hormone was discovered. Additionally, it had been prevalently known that exercise does not reduce food intake but burns fat and calories, but the molecular mechanism of this

* Corresponding author: mkizil@firat.edu.tr
0030-9923/2022/0001-0001 \$ 9.00/0



Copyright 2022 by the authors. Licensee Zoological Society of Pakistan.

This article is an open access  article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Article Information

Received 31 October 2022

Revised 18 December 2022

Accepted 02 January 2023

Available online 23 February 2023
(early access)

Authors' Contribution

MK and AR designed the study and performed all the experimental work. MA, TŞ, MAK, ÖY and BFY collected the blood samples. İŞ carried out the statistical analysis. The manuscript was written by MK.

Key words

Adiponectin, Asprosin, Calf, Irisin, Leptin

process could not be explained until the discovery of irisin (Boström *et al.*, 2012). Therefore, the isolation of irisin has helped to explain metabolic events to a large extent (Polyzos *et al.*, 2013).

Asprosin is a newly discovered adipokine that increases appetite by triggering hepatic glucose release. A C-terminal cleavage product of the profibrillin-1 protein (encoded by the FBN1 gene), asprosin is a hormone in a protein form that modulates hepatic glucose release and has higher secretion rates during hunger. Several important hormones that take part in metabolism and energy homeostasis are secreted from adipose tissue, but asprosin is mainly secreted from white adipose tissue (Romere *et al.*, 2016). It was emphasized that asprosin levels have a positive relationship with insulin resistance, body mass index, and free androgen index (Alan *et al.*, 2019).

Leptin is a recently discovered metabolic hormone, and knowledge of its significance is increasing day by day (Peelman *et al.*, 2004). The most important function of leptin is keeping the amount of fat in the body fixed (Klaus, 2004). Leptin accelerates the maturation of female reproductive organs and is a required hormone for pregnancy (Chehab *et al.*, 1996; Malik *et al.*, 2001).

Adiponectin is a collagen-like plasma protein that is synthesized from connective tissue (Looker *et al.*, 2004). Plasma adiponectin levels are noticeably lower in men than women, and adiponectin expression is higher in subcutaneous adipose tissue than visceral adipose tissue (Nishizawa *et al.*, 2002). High adiponectin levels in newborns may originate from the different distributions of their fat storage sites (Sivan *et al.*, 2003).

Insulin-like growth factor-1 (IGF-1) is an insulin-like hormone that has growth effects in childhood and anabolic effects in adults. It is produced primarily by the liver as an endocrine hormone and by target tissues in a paracrine/autocrine manner. The growth function in animals is controlled by a complicated system where the somatotrophic axis plays a highly effective role (Deng *et al.*, 2010). It was suggested that growth hormones including IGF-1 regulate muscle and bone growth in this axis and are mainly responsible for postnatal growth (Sellier, 2000).

The aim of this study was to determine the levels of irisin, asprosin, leptin, adiponectin, and IGF-1 in cows and the umbilical cord during labor, to determine the effects of the mode of delivery on these hormones, and to identify changes in these hormones in calves after birth.

MATERIALS AND METHODS

Animals

This study was conducted after obtaining approval from the Experimental Animals Ethics Committee

of Bingöl University (decision number: 1199; date: 11/05/2020). The study was carried out with 20 clinically healthy Holstein cows at the ages of 3-5 years that had given birth once in a private establishment in the province of Bingöl, Turkey, as well as 20 calves born from these cows. In the establishment, the cows were milked in the morning and evening with automated milking machines, and a semi-open feeding system was used. The average daily milk yield of the cows was 25 liters, and they were fed with rations consisting of concentrate feed containing barley and roughage comprising dry meadow grass, maize silage, alfalfa, and hay. Body condition scores ranged from 3.4 to 3.5. The calves were fed with substitute feed from the 30th day after birth.

Experimental model

The 20 cows and calves included were randomly divided into 4 groups as follows. Vaginal, dystocia, preterm and cesarean section group consists of 5 cows and 5 calves born from these cows in each group. The weights of the included calves were measured based on the blood collection schedule. Throughout the study, the health statuses of the calves were recorded. The cows for which spontaneous vaginal birth did not occur in a species-specific period or those that could not give birth without any assistance were selected as the dystocia group, while those that gave birth between the 220th and 270th days of gestation were selected as the preterm group (Musal and Koker, 2019).

Blood sample collection and analyses

Using 10-ml tubes, blood samples were collected from the vena jugularis of all cows during labor before the calf came out and from the umbilical cord right after the calf came out. The sera of these blood samples were separated for analyses. Blood samples were also collected in 10-ml tubes from the calves in all groups during labor, after they drank colostrum, and on the 15th, 30th, 45th, and 60th days in the postnatal period. The sera of the samples were separated and kept at -80°C until the analyses.

Determination of irisin, asprosin, leptin, adiponectin, and IGF-1 levels

Commercial ELISA kits were used to determine levels of the following in the collected serum samples: Irisin (SunRed bovine irisin ELISA kit catalog no: DZE201042917), asprosin (SunRed bovine asprosin ELISA kit catalog no: DZE201043068), leptin (SunRed bovine leptin ELISA kit catalog no: DZE201040174), adiponectin (SunRed bovine adiponectin ELISA kit catalog no: DZE201040211), and IGF-1 (SunRed bovine IGF-1 ELISA kit catalog no: DZE201040024). Levels

were determined based on the manufacturer's instructions and an ELISA reader (Bio Tek Instruments, Winooski, VT, USA).

Statistical analyses

The number of animals to be used in the study was determined by conducting power analyses with a 98% confidence interval. This ensured that the groups in the study formed a single paired group, and blood was collected from the same animals 6 times. The normality of the distributions was tested in the irisin, asprosin, leptin, adiponectin, and IGF-1 data using visual methods (histograms and probability plots) and the Shapiro-Wilk test. As a result of the tests, it was determined all data were non-normally distributed and failed to meet parametric test conditions. Therefore, for

all parameters, the groups were compared using the non-parametric Kruskal-Wallis test. After the Kruskal-Wallis test, the Mann-Whitney U test with Bonferroni correction was used in post-hoc pairwise comparisons ($p < 0.05$). The Wilcoxon test was used as a dependency test ($p < 0.05$) in the comparisons of the maternal blood and umbilical cord blood samples of the groups. The Friedman test was used for the comparisons of all parameters for the pre-colostrum, post-colostrum, 15th day, 30th-day, 45th-day and 60th-day periods for the calves of separate cows for each of the groups. The Wilcoxon test was used for the post-hoc pairwise comparisons after the Friedman test ($p < 0.05$) (Akgül, 2005). The statistical analyses were carried out using SPSS 22 (Statistical Package for the Social Sciences for Windows, Chicago, Illinois, USA).

Table I. The levels of irisin, asprosin, leptin, adiponectin and IGF-1 in all groups of the study.

Groups	Cow (n=5)	Umbilical cord (n=5)	P	Before colostrum (n=5)	After colostrum (n=5)	15 th day	30 th day	45 th day	60 th day	p
Irisin (ng/ml)										
VD	0.66±0.09	1.36±0.23	0.043	1.64±0.11 ^{abBC}	1.18±0.18 ^{BC}	0.90±0.15 ^A	1.26±0.53 ^{ABC}	1.00±0.10 ^{AB}	0.98±0.14 ^{AB}	0.037
Dystocia	0.64±0.08	1.52±0.31	0.068	2.34±0.29 ^{bcC}	1.32±0.18 ^{AB}	1.02±0.12 ^A	1.12±0.17 ^{AB}	1.24±0.16 ^{AB}	1.44±0.18 ^B	0.005
Preterm	0.83±0.14	1.48±0.27	0.042	1.40±0.23 ^a	1.18±0.17	0.70±0.13	0.90±0.13	0.96±0.09	1.02±0.04	0.117
Cesarean	0.56±0.13	2.54±0.46	0.042	2.62±0.34 ^{cB}	0.86±0.05 ^A	0.74±0.04 ^A	0.86±0.08 ^A	0.92±0.17 ^A	0.88±0.07 ^A	0.016
p	0.507	0.164		0.006	0.189	0.152	0.492	0.258	0.081	
Asprosin (ng/ml)										
VD	0.58±0.13	1.08±0.08	0.043	1.08±0.10	0.68±0.17	0.62±0.12	0.56±0.10	0.76±0.20	0.74±0.14	0.107
Dystocia	0.64±0.06	1.04±0.27	0.225	1.32±0.20	1.02±0.15	0.88±0.28	0.94±0.06	0.98±0.06	0.82±0.07	0.311
Preterm	0.48±0.08	1.04±0.12	0.043	1.02±0.19	0.80±0.14	0.50±0.12	0.72±0.08	0.62±0.12	0.72±0.08	0.068
Cesarean	0.50±0.03	1.16±0.23	0.043	1.20±0.09 ^B	0.82±0.11 ^{AB}	0.74±0.06 ^A	0.76±0.09 ^A	0.74±0.06 ^A	0.86±0.11 ^{AB}	0.037
p	0.381	0.963		0.140	0.308	0.517	0.054	0.133	0.522	
Leptin (ng/ml)										
VD	0.64±0.09 ^{ab}	2.12±0.26	0.041	1.72±0.30	1.66±0.45	0.90±0.20 ^a	0.98±0.22 ^a	1.30±0.26	1.10±0.28 ^a	0.233
Dystocia	1.16±0.16 ^c	2.08±0.35	0.136	2.14±0.42	2.26±0.21	2.26±0.12 ^b	2.16±0.16 ^c	1.46±0.32	2.56±0.05 ^b	0.132
Preterm	1.02±0.21 ^{bc}	2.86±0.23	0.043	1.66±0.36	1.92±0.43	0.78±0.15 ^a	1.26±0.21 ^{ab}	0.74±0.04	1.10±0.19 ^a	0.164
Cesarean	0.30±0.10 ^a	2.56±0.12	0.043	1.78±0.45	1.70±0.07	1.20±0.31 ^a	1.60±0.15 ^{bc}	0.62±0.30	1.50±0.35 ^a	0.173
p	0.009	0.298		0.847	0.389	0.008	0.017	0.176	0.007	
Adiponektin (ng/ml)										
VD	2.46±0.39	5.52±0.80	0.043	3.64±0.49	3.14±0.52	2.46±0.46 ^a	2.44±0.26 ^a	2.50±0.18	2.56±0.18	0.470
Dystocia	2.86±0.32	3.76±1.24	0.686	5.80±1.53	6.08±0.37	4.60±0.73 ^b	6.38±0.42 ^c	4.88±1.25	5.46±1.38	0.504
Preterm	2.56±0.55	9.08±3.88	0.080	3.50±1.08	4.18±0.75	2.36±0.24 ^a	2.88±0.47 ^a	2.92±0.04	2.56±0.27	0.434
Cesarean	2.22±0.57	6.20±0.48	0.043	5.12±0.76	4.54±1.02	2.38±0.63 ^a	4.60±0.74 ^b	2.80±0.87	4.64±1.12	0.080
p	0.609	0.428		0.232	0.059	0.025	0.008	0.204	0.170	
IGF-1 (ng/ml)										
VD	49.20±5.98	57.00±4.27 ^a	0.138	81.00±16.40 ^{aF}	44.60±2.31 ^{aABCD}	53.00±5.41 ^{abDEF}	40.60±3.81 ^{aAB}	47.00±1.44 ^{aBE}	40.60±1.88 ^{aACD}	0.007
Dystocia	68.00±7.67	109.40±20.75 ^{bc}	0.225	149.80±13.13 ^{bc}	102.20±7.51 ^{bBC}	73.80±5.7 ^{bcA}	85.20±0.86 ^{bAB}	96.80±6.28 ^{bb}	109.40±8.24 ^{bbc}	0.004
Preterm	49.20±8.52	80.00±16.60 ^{ab}	0.043	58.20±8.39 ^a	55.40±9.24 ^a	49.40±6.90 ^a	48.60±5.97 ^a	56.60±5.24 ^a	53.60±4.92 ^a	0.456
Cesarean	56.00±5.26	141.20±10.56 ^c	0.043	121.60±10.06 ^b	89.40±7.61 ^b	87.20±9.39 ^c	79.20±4.97 ^b	86.40±8.10 ^b	96.80±9.23 ^b	0.097
p	0.236	0.027		0.005	0.003	0.017	0.002	0.002	0.002	

a, b, c the difference between groups with different letters in the same column is statistically significant ($p < 0.05$). A, B, C, D, E, F the difference between groups with different letters on the same line is statistically significant ($p < 0.05$). VD, Vaginal deliver.

RESULTS

The results of irisin, asprosin, leptin, adiponectin and IGF-1 analyses are shown in [Table I](#). [Table I](#) shows that the irisin levels in the maternal blood samples of the vaginal delivery, dystocia, preterm, and cesarean section groups were 0.66 ± 0.09 ng/ml, 0.64 ± 0.08 ng/ml, 0.83 ± 0.14 ng/ml, and 0.56 ± 0.13 ng/ml, respectively. The umbilical-cord irisin levels were significantly higher than the maternal irisin levels in the vaginal delivery ($P < 0.043$), preterm ($P < 0.042$), and cesarean section ($P < 0.042$) groups. The pre-colostrum irisin levels in the calves in all groups were higher than their post-colostrum levels, and the differences in the dystocia and cesarean section groups were statistically significant.

DISCUSSION

Adipokines have highly complicated effects on the body, and the effects of each one on the organism vary under different conditions. This complicated nature is leading to the discovery of different results in different studies ([Mehta and Farmer, 2007](#)).

Irisin has multi-spectrum functions, including the conversion of white adipose tissue to brown adipose tissue, reduction of insulin resistance, and improvement of muscle-bone connectivity. Brown adipose tissue is very important for thermogenesis in the neonatal period and is essential for newborn survival ([Ojha *et al.*, 2013](#)). Brown adipose tissue creates heat rapidly by increasing energy consumption, thus providing protection against hypothermia that could occur in the extrauterine environment ([Cannon and Nedergaard, 2004](#); [Asakura, 2004](#)). For this reason, irisin may have a role in the thermoregulation mechanisms of the newborn, and its presence in the colostrum may contribute to thermoregulation after birth. A previous study reported that lower irisin concentrations are found in the colostrum during breastfeeding because the mother consumes more energy in this process ([Briana *et al.*, 2017](#)). The source of irisin in human colostrum is not yet known. Lower concentrations of irisin in comparison to maternal serum levels may indicate the transfer of irisin from the mother's circulation to the milk. Consequently, although the exact location of its production has not been determined yet, it has been demonstrated that colostrum contains irisin. Therefore, it is strongly recommended that infants be breastfed early, especially infants born via cesarean section who are prone to hypothermia, respiratory dysfunctions, and dehydration ([Briana *et al.*, 2017](#)). A study that carried out with Holstein bulls found FNDC5 in cattle skeletal muscles, but despite substantial differences in body composition, neither FNDC5 nor irisin were

detected in circulation under standard animal husbandry conditions ([Komolka *et al.*, 2014](#)). It was indicated that the modulatory, molecular, and physiological roles of FNDC5/irisin are not exactly defined yet, there are various conflicting findings on this issue, and there is a serious need to investigate the functional mechanisms of FNDC5/irisin in mammals ([Wu *et al.*, 2021](#)). One study investigated maternal and cord blood irisin levels in mothers with preterm and term deliveries. Irisin levels were significantly higher in maternal peripheral blood (11.6 ± 2.0 ng/ml) than cord blood (7.2 ± 1.9 ng/ml). However, irisin levels of maternal peripheral blood were not significantly different ([Pavlova *et al.*, 2018](#)). Another study found mean serum irisin levels of 393 ng/ml and 333.2 ng/ml in maternal and cord blood samples, respectively ([Yuksel *et al.*, 2014](#)). [Haberal *et al.* \(2017\)](#) compared the effects of vaginal delivery with an elective cesarean section on irisin levels. No statistically significant differences were determined in irisin levels in either maternal serum or in cord blood between the cesarean section and vaginal delivery groups. They also suggested that mean irisin levels in cord blood were similar to those of maternal blood. In our study, the irisin levels in umbilical-cord blood were significantly higher than in the maternal blood in all groups except for the dystocia group. Considering that peptide hormones cannot cross the placental barrier ([Vaughan and Fowde, 2016](#)), the increase in irisin levels in umbilical-cord blood indicates the presence of a highly significant level of irisin synthesis in the fetus. A previous study reported lower irisin levels in cord blood samples from newborns with intrauterine growth restriction, which may result in less browning of their adipose tissue ([Briana *et al.*, 2014](#)). In our study, growth retardation was not observed in any of the calves in all groups, and it was determined that all of them were healthy. Although the number of subjects in this study was very low, the occurrence of high levels of irisin in the fetus suggested that irisin can have positive effects on the intrauterine development of calves. The activity and serum concentration of irisin depend on the physiological and/or pathological state ([Korta *et al.*, 2019](#)). In this study, irisin levels decreased in the blood samples collected from the calves after colostrum intake (on the 15th, 30th, 45th, and 60th days). Irisin levels in circulation increased during labor and right after birth to facilitate thermoregulation and may have declined to normal levels with better functioning of homeostasis in the following days.

[Kılinc and Risvanli \(2022\)](#) found postpartum asprosin concentrations of 0.99 ± 0.41 ng/ml in sick cows, which was significantly higher than the level of 0.86 ± 0.27 ng/ml in healthy cows. In this study, the asprosin levels in maternal and umbilical-cord blood are in agreement with the data from [Kılinc and Risvanli \(2022\)](#). Another study did not

identify any significant difference between the asprosin levels of blood serum samples collected from healthy mothers, umbilical-cord blood, and calves (Baykus *et al.*, 2019). In this study, the asprosin levels in cord blood of the vaginal delivery, preterm, and cesarean section groups were significantly higher than the levels in maternal blood. This increase may have been caused by the calves' glucose needs being met calves during labor. Asprosin has lower concentrations in milk samples of women than their plasma samples. However, no other study has determined asprosin levels in colostrum. Asprosin levels pathologically increase in conditions such as obesity, insulin resistance, and diabetes mellitus (Morcos *et al.*, 2022). In our study, the increase in the asprosin levels of cord blood in the vaginal delivery, preterm, and cesarean section groups was not high, and there was a gradual decrease in the serum levels of asprosin in calves until the 60th day after birth.

Leptin regulates the balance between energy intake and energy utilization and ultimately plays a role in fetal growth (Christou *et al.*, 2002; Lewandowski *et al.*, 1999). Maternal leptin levels significantly increase in mid-pregnancy and during labor and then reach the physiological levels of non-pregnant woman by 3 to 6 days after delivery (Nuamah *et al.*, 2004). Leptin levels in cord blood increase with advancing pregnancy and peak after 37–40 weeks of gestation (Kang *et al.*, 2020). High leptin levels in cord blood suggest that the fetus is capable of leptin production in adipose tissue. Additionally, placental leptin synthesis and secretion may contribute to the high levels of leptin in umbilical-cord plasma (Senaris *et al.*, 1997). Increased leptin levels in cord blood may provide a physiological advantage to newborn infants by limiting energy consumption by the body and preserving nutrient reserves for growth and development (Gualillo *et al.*, 2001). Similarly, in our study, the leptin concentrations in umbilical-cord blood of the vaginal delivery, preterm, and cesarean section groups were significantly higher than those in maternal blood. Leptin levels in the placenta are indicated as a cause of higher leptin levels in maternal blood than cord blood. It has been shown that leptin levels in cord blood in the vaginal delivery group were higher than in the cesarean section delivery group, indicating an augmented placental release of leptin during advanced labor (Yoshimitsu *et al.*, 2000). Fetuses delivered vaginally are prone to undergoing more stress during labor than those delivered by cesarean section (Yoshimitsu *et al.*, 1999). The findings of these studies are supported by the increase in the leptin levels of the calves after colostrum intake in the present study

Adiponectin is abundant in cord blood, where levels are higher than those of maternal circulation, indicating a potential regulatory role in fetal development (Weyermann

et al., 2006; Luo *et al.*, 2013). In contrast, Shen *et al.* (2019) showed that adiponectin levels in venous blood of cows are higher than those of cord venous blood. In our study, adiponectin levels in cord blood from all groups were higher than the maternal-blood levels, in contrast to the findings of Shen *et al.* (2019) but similar to other findings (Weyermann *et al.*, 2006; Luo *et al.*, 2013). This difference was significant in the vaginal delivery and cesarean section groups. High fetal adiponectin concentrations may be largely attributable to adiponectin secretion by fetal adipose tissue (Mazaki-Tovi *et al.*, 2007). The placenta might also be a source of adiponectin. It has been revealed that adiponectin is expressed in the placenta and secreted in both maternal and fetal blood circulation (Chen *et al.*, 2006). In another study, adiponectin levels were significantly lower in infants born by elective cesarean section than those born by vaginal delivery (Hermansson *et al.*, 2014). Nevertheless, these inconsistencies are believed to appear as a result of very few studies having been conducted on this topic (Nobe *et al.*, 2013). The adiponectin concentrations in serum samples of newborn calves are substantially increased at 24 h after colostrum intake (Kesser *et al.*, 2015). In our study, no significant change was seen in the blood serum adiponectin levels of the calves between before and after colostrum intake. This different result may have originated from differences in times of blood-sample collection.

IGF-1 is primarily derived from the liver, but its main source is the placenta during gestation. A previous study determined the mean IGF-1 level was 44.7 ± 7.6 ng/ml in cows that had given healthy births at 24 h after delivery. The highest levels were determined in the dry period with a mean value of 113.7 ± 3.1 ng/ml. In the present study, the IGF-1 levels of the cows that gave birth with different modes of delivery were similar to those reported in the literature (Aribat *et al.*, 1990). Maternal IGF-1 levels have demonstrated to be higher than those in cord blood (Higgins *et al.*, 2012). The lower IGF-1 levels of the cows in our study may have been caused by different factors during labor. IGF-1 levels in the circulation of cows decreases noticeably during labor in comparison to the dry period. The lower IGF-1 concentration during labor could be caused by the transfer of IGF-1 from the mother to the colostrum and the negative energy balance forming in the mother in this process (excessive losses of IGF-1 through colostrum and the insufficient energy supply are possibly responsible for the decrease during the colostrum period) (Ronge and Blum, 1988). In our study, the mode of delivery had different effects on the fetal IGF-1 levels. The IGF-1 levels of the cesarean section and dystocia groups were significantly higher than those in the vaginal delivery group. Because IGF-1 cannot pass from the mother to

the fetus through the placenta, maternal IGF-1 levels have an indirect impact on fetal growth (Davidson *et al.*, 2006). Ronge and Blum (1988) reported very high IGF-1 concentrations in colostrum-much higher than in the blood of cows-indicating strong active transport and/or local production in the mammary tissue. However, colostrum feeding did not increase IGF-1 levels in the blood of calves on the first day after delivery. In this study, the highest value IGF-1 level was obtained in the cord blood samples from the cesarean section group at, while the lowest values were found in the vaginal delivery group at and the preterm group at. The maternal-blood IGF-1 levels of the cows in our study were compatible with values reported in the literature (Rhoads *et al.*, 2008). Among the IGF-1 levels of the calves born by vaginal delivery, dystocia, preterm, and cesarean section, the highest value was found in the dystocia group before colostrum intake as whereas the lowest value was found in the vaginal delivery group on the 30th day. In the previous studies (Lents *et al.*, 1998; Panzani *et al.*, 2017) reported they were lower in the period after colostrum intake. In parallel with those findings, Probo *et al.* (2010) also reported a decline in IGF-1 levels of calves from the 30th minute after birth to the 6th day in the postnatal period. The IGF-1 levels identified in the calves in our study right after birth also had a downward trend through the following sample collection periods (15th, 30th, 45th, and 60th days), and these results were compatible with the information in the literature. It was proposed that the reason for lower levels after birth could be the insufficient production of IGF-1 in the liver in that period or its inadequate absorption (Panzani *et al.*, 2017). Furthermore, the reason for the lowest IGF-1 levels in the calves in the preterm group in this study was thought to be not only insufficient maternal and fetal production, but also inadequate absorption.

CONCLUSION

The results of this study indicate that the mode of delivery does not have a prominent impact on irisin, asprosin, leptin, adiponectin and IGF-1 levels in both maternal and fetal blood. The higher levels all the hormones in cord bloods suggest that these hormones may have important functions in fetal life. Further studies are needed to determine the effects of these hormones in fetal development.

ACKNOWLEDGEMENT

The authors would like to acknowledge the financial support of The Scientific and Technological Research Council of Turkey (TUBITAK, Grant No: 1200760).

Funding

This work was supported by the Scientific and Technological Research Council of Turkey (Project no: TUBİTAK-1200760)

IRB approval

Not applicable

Ethical statement

This study was approved by the Bingöl University Animal Experiments Local Ethics Committee (Approval no: 2020/1199).

Statement of conflict of interest

The authors have declared no conflict of interest.

REFERENCES

- Abribat, T., Lapiere, H., Dubreuil, P., Pelletier, G., Gaudreau, P., Brazeau, P. and Petitclerc, D., 1990. Insulin-like growth factor-I concentration in Holstein female cattle: variations with age, stage of lactation and growth hormone-releasing factor administration. *Domest. Anim. Endocrinol.*, **7**: 93-102. [https://doi.org/10.1016/0739-7240\(90\)90058-8](https://doi.org/10.1016/0739-7240(90)90058-8)
- Ahima, R.S. and Flier, J.S., 2000. Adipose tissue as an endocrine organ. *Trends Endocrinol. Metabol.*, **11**: 327-332. [https://doi.org/10.1016/S1043-2760\(00\)00301-5](https://doi.org/10.1016/S1043-2760(00)00301-5)
- Akgül, A., 2005. *Tıbbi Araştırmalarda İstatistiksel Analiz Teknikleri*. SPSS Uygulamaları. Emek Ofset: Ankara, Türkiye.
- Alan, M., Gurlek, B., Yılmaz, A., Aksit, M., Aslanipour, B., Gülhan, I., Calan, M. and Cuneyt, E.T., 2019. Asprosin: A novel peptide hormone related to insulin resistance in women with polycystic ovary syndrome. *Gynecol. Endocrinol.*, **35**: 220-223. <https://doi.org/10.1080/09513590.2018.1512967>
- Asakura, H., 2004. Fetal and neonatal thermoregulation. *J. Nippon med. Sch.*, **71**: 360-370. <https://doi.org/10.1272/jnms.71.360>
- Baykuş, Y., Yavuzkır, S., Ustebay, S., Ugur, K., Deniz, R. and Aydın, S., 2019. Asprosin in umbilical cord of newborns and maternal blood of gestational diabetes, preeclampsia, severe preeclampsia, intrauterine growth retardation and macrosomic fetus. *Peptides*, **120**: 170132. <https://doi.org/10.1016/j.peptides.2019.170132>
- Boström, P., Wu, J., Jedrychowski, M. and Korde, A., 2012. Irisin induces brown fat of white adipose tissue in vivo and protects against diet-induced

- obesity and diabetes. *Nature*, **481**: 463-468. <https://doi.org/10.1038/nature10777>
- Briana, D., Malamitsi-Puchner, A., Boutsikou, M., Baka, S., Ristani, A., Hassiakos, D., Gourgiotis, D. and Boutsikou, T., 2014. PS-042 myokine irisin is down-regulated in fetal growth restriction. *Arch. Dis. Child.*, **99**: A126. <https://doi.org/10.1136/archdischild-2014-307384.336>
- Briana, D.D., Boutsikou, M., Boutsikou, T., Marmarinos, A., Gourgiotis, D. and Malamitsi-Puchner, A., 2017. Novel bioactive substances in human colostrum: Could they play a role in postnatal adaptation? *J. Matern. Fetal Neonatal Med.*, **30**: 504-507. <https://doi.org/10.1080/14767058.2016.1177817>
- Cannon, B. and Nedergaard, J., 2004. Brown adipose tissue: Function and physiological significance. *Physiol. Rev.*, **84**: 277-359. <https://doi.org/10.1152/physrev.00015.2003>
- Chehab, F.F., Lim, M.E., and Lu, R., 1996. Correction of the sterility defect in homozygous obese female mice by treatment with the human recombinant leptin. *Nat. Genet.*, **12**: 318-320. <https://doi.org/10.1038/ng0396-318>
- Chen, J., Tan, B., Karteris, E., Zervou, S., Digby, J., Hillhouse, E.W., Vathish, M. and Randevara, H.S., 2006. Secretion of adiponectin by human placenta: Differential modulation of adiponectin and its receptors by cytokines. *Diabetologia*, **49**: 1292-1302. <https://doi.org/10.1007/s00125-006-0194-7>
- Christou, H., Serdy, S. And Mantzoros, C.S., 2002. Leptin in relation to growth and developmental processes in the fetus. *Semin. Reprod. Med.*, **20**: 123-130. <https://doi.org/10.1055/s-2002-32503>
- Davidson, S., Hod, M., Merlob, P. and Shtaf, B., 2006. Leptin, insulin, insulin-like growth factors and their binding proteins in cord serum: Insight into fetal growth and discordancy. *Clin. Endocrinol.*, **65**: 586-592. <https://doi.org/10.1111/j.1365-2265.2006.02632.x>
- Deng, C., Ma, R., Yue, X., Lan, X., Chen, H. and Lei, C., 2010. Association of IGF-I gene polymorphisms with milk yield and body size in Chinese dairy goats. *Gen. mol. Biol.*, **33**: 266-270. <https://doi.org/10.1590/S1415-47572010005000034>
- Dua, A., Hennes, M.I., Hoffmann, R.G., Maas, D.L., Krakower, G.R., Sonnenberg, G.E. and Kissebah, A.H. 1996. Leptin: A significant indicator of total body fat but not of visceral fat and insulin insensitivity in African-American women. *Diabetes*, **45**: 1635-1637. <https://doi.org/10.2337/diab.45.11.1635>
- Gualillo, O., Caminos, J.E., Blanco, M., García-Caballero, T., Kojima, M., Kangawa, K., Dieguez, C. and Casanueva, F., 2001. Ghrelin, a novel placental-derived hormone. *Endocrinology*, **142**: 788-794. <https://doi.org/10.1210/endo.142.2.7987>
- Haberal, E.T., Ulu, İ., Özcan, C., Gök, G.A., Kıran, G. and Kucur, M., 2017. Is there a relationship between delivery mode and serum irisin levels in pregnant women? *J. Lab. Med.*, **41**: 317-323. <https://doi.org/10.1515/labmed-2017-0042>
- Hermansson, H., Hoppu, U. and Isolauri, E., 2014. Elective caesarean section is associated with low adiponectin levels in cord blood. *Neonatology*, **105**: 172-174. <https://doi.org/10.1159/000357178>
- Higgins, M.F., Russell, N.E., Crossey, P.A., Nyhan, K.C., Brazil, D.P. and McAuliffe, F.M., 2012. Maternal and fetal placental growth hormone and IGF axis in type 1 diabetic pregnancy. *PLoS One*, **7**: e29164. <https://doi.org/10.1371/journal.pone.0029164>
- Kang, S.J., Bae, J.G., Kim, S. and Park, J.H., 2020. Birth anthropometry and cord blood leptin in Korean appropriate-for-gestational-age infants born at \geq 28 weeks' gestation: A cross sectional study. *Int. J. Pediatr. Endocrinol.*, **2020**: 1-6. <https://doi.org/10.1186/s13633-020-00082-6>
- Kesser, J., Hill, M., Heinz, J., Koch, C., Rehage, J., Steinhoff-Wagner, J., Hammon, H., Mielenz, B., Sauerwein, H. and Sadri, H., 2015. The rapid increase of circulating adiponectin in neonatal calves depends on colostrum intake. *J. Dairy Sci.*, **98**: 7044-7051. <https://doi.org/10.3168/jds.2015-9726>
- Kılınc, M.A. and Risvanlı, A., 2022. The relationship of asprosin with β -hydroxybutyric acid and postpartum disorders in cows. *Acta Vet. Hung.*, **70**: 58-63. <https://doi.org/10.1556/004.2022.00002>
- Klaus, S., 2004. Adipose tissue as a regulator of energy balance. *Curr. Drug Targets*, **5**: 241-250. <https://doi.org/10.2174/1389450043490523>
- Komolka, K., Albrecht, E., Schering, L., Brenmoehl, J., Hoefflich, A. and Maak, S., 2014. Locus characterization and gene expression of bovine FNDC5: Is the myokine irisin relevant in cattle? *PLoS One*, **9**: e88060. <https://doi.org/10.1371/journal.pone.0088060>
- Korta, P., Pocheć, E. and Mazur-Biały, A., 2019. Irisin as a multifunctional protein: Implications for health and certain diseases. *Medicina*, **55**: 485. <https://doi.org/10.3390/medicina55080485>
- Lents, C., Wettemann, M., Looper, M., Bossis, I., Spicer, L. and Vizcarra, J., 1998. Concentrations of GH, IGF-I, Insulin, and glucose in postnatal beef

- calves. *Anim. Sci. Res. Rep.*, pp. 215-222.
- Lewandowski, K., Horn, R., O'Callaghan, C.J., Dunlop, D., Medley, G.F., O'Hare, P., and Brabant, G., 1999. Free leptin, bound leptin, and soluble leptin receptor in normal and diabetic pregnancies. *J. Clin. Endocrinol. Metab.*, **84**: 300-306. <https://doi.org/10.1210/jcem.84.1.5401>
- Lidell, M.E. and Enerbäck, S., 2010. Brown adipose tissue a new role in humans? *Nat. Rev. Endocrinol.*, **6**: 319-325. <https://doi.org/10.1038/nrendo.2010.64>
- Looker, H.C., Krakoff, J., Funahashi, T., Matsuzawa, Y., Tanaka, S., Nelson, R.G., Knowler, W.C., Lindsay, R.S. and Hanson, R.L., 2004. Adiponectin concentrations are influenced by renal function and diabetes duration in Pima Indians with type 2 diabetes. *J. clin. Endocrinol. Metab.* **89**: 4010-4017. <https://doi.org/10.1210/jc.2003-031916>
- Luo, Z.C., Nuyt, A.M., Delvin, E., Fraser, W.D., Julien, P., Audibert, F., Girard, I., Shatenstein, B., Deal, C. and Grenier, E., 2013. Maternal and fetal leptin, adiponectin levels and associations with fetal insulin sensitivity. *Obesity*, **21**: 210-216. <https://doi.org/10.1002/oby.20250>
- Malik, N., Carter, N.D., Murray, J.F., Scaramuzzi, R., Wilson, C. and Stock, M., 2001. Leptin requirement for conception, implantation, and gestation in the mouse. *Endocrinology*, **142**: 5198-5202. <https://doi.org/10.1210/endo.142.12.8535>
- Mazaki-Tovi, S., Kanety, H., Pariente, C., Hemi, R., Efraty, Y., Schiff, E., Shoham, A. and Sivan, E., 2007. Determining the source of fetal adiponectin. *J. Reprod. Med.*, **52**: 774-778.
- Mehta, S. and Farmer, J.A., 2007. Obesity and inflammation: a new look at an old problem. *Curr. Atheroscler. Rep.*, **9**: 134-138. <https://doi.org/10.1007/s11883-007-0009-4>
- Morcos, Y.A., Lütke, S., Tenbrieg, A., Hanisch, F.G., Prymachuk, G., Piekarek, N., Hoffmann, T., Keller, T., Janoschek, R., Niehoff, A., 2022. Sensitive asprosin detection in clinical samples reveals serum/saliva correlation and indicates cartilage as source for serum asprosin. *Sci. Rep.*, **12**: 1-19. <https://doi.org/10.1038/s41598-022-05060-x>
- Musal, B. and Köker, A., 2019. Dystocia. In: *Obstetrics and gynecology in farm animals* (eds. M. Kaymaz, A. Semacan, M. Findik, A. Rişvanlı, and A. Köker). 3rd ed, Medipres, Malatya. pp. 187-234.
- Nishizawa, H., Shimomura, I., Kishida, K., Maeda, N., Kuriyama, H., Nagaretani, H., Matsuda, M., Kondo, H., Furuyama, N. and Kihara, S., 2002. Androgens decrease plasma adiponectin, an insulin-sensitizing adipocyte-derived protein. *Diabetes*, **51**: 2734-2741. <https://doi.org/10.2337/diabetes.51.9.2734>
- Nobe, K., Fujii, A., Saito, K., Negoro, T., Ogawa, Y., Nakano, Y., Hashimoto, T. and Honda, K., 2013. Adiponectin enhances calcium dependency of mouse bladder contraction mediated by protein kinase Ca expression. *J. Pharmacol. exp. Ther.*, **345**: 62-68. <https://doi.org/10.1124/jpet.112.202028>
- Nuamah, M.A., Yura, S., Sagawa, N., Itoh, H., Mise, H., Korita, D., Kakui, K., Takemura, M., Ogawa, Y. and Nakao, K., 2004. Significant increase in maternal plasma leptin concentration in induced delivery: A possible contribution of pro-inflammatory cytokines to placental leptin secretion. *Endocr. J.*, **51**: 177-187. <https://doi.org/10.1507/endocrj.51.177>
- Ojha, S., Robinson, L., Yazdani, M., Symonds, M.E. and Budge, H., 2013. Brown adipose tissue genes in pericardial adipose tissue of newborn sheep are downregulated by maternal nutrient restriction in late gestation. *Pediatr. Res.*, **74**: 246-251. <https://doi.org/10.1038/pr.2013.107>
- Panzani, S., Carluccio, A., Faustini, M., Prandi, A., Probo, M., and Veronesi, M.C., 2017. Comparative study on insulin-like growth factor I (IGF-I) plasma concentrations in new-born horse foals, donkey foals and calves. *Fetal. Neonatal. Dev. Med.*, **1**: 1-6. <https://doi.org/10.15761/FNDM.1000103>
- Pavlova, T., Zlamal, F., Tomandl, J., Hodicka, Z., Gulati, S. and Bienertova-Vasku, J., 2018. Irisin maternal plasma and cord blood levels in mothers with spontaneous preterm and term delivery. *Dis. Markers*, **2018**: 7628957. <https://doi.org/10.1155/2018/7628957>
- Peelman, F., Waelput, W., Iserentant, H., Lavens, D., Eyckerman, S., Zabeau, L. and Tavernier, J., 2004. Leptin: Linking adipocyte metabolism with cardiovascular and autoimmune diseases. *Prog. Lipid Res.*, **43**: 283-301. <https://doi.org/10.1016/j.plipres.2004.03.001>
- Polyzos, S.A., Kountouras, J., Shields, K. and Mantzoros, C.S., 2013. Irisin: A renaissance in metabolism? *Metabolism*, **62**: 1037-1044. <https://doi.org/10.1016/j.metabol.2013.04.008>
- Probo, M., Comin, A., Faustini, M., Prandi, A. and Veronesi, M., 2010. Insulin-like growth factor I and non esterified fatty acids plasma concentrations in the newborn calf. *14th Ann. Conf. Eur. Soc. Reprod. Domest. Anim.*, **45**: 70.
- Rhoads, M., Meyer, J., Kolath, S., Lamberson, W. and Lucy, M., 2008. Growth hormone receptor, insulin-like growth factor (IGF)-1, and IGF-binding protein-2 expression in the reproductive tissues of early postpartum dairy cows. *J. Dairy Sci.*, **91**:

- 1802-1813. <https://doi.org/10.3168/jds.2007-0664>
- Romere, C., Duerschmid, C., Bournat, J., Constable, P., Jain, M., Xia, F., Saha, P.K., Del Solar, M., Zhu, B. and York, B., 2016. Asprosin, a fasting-induced glucogenic protein hormone. *Cell*, **165**: 566-579. <https://doi.org/10.1016/j.cell.2016.02.063>
- Ronge, H. and Blum, J., 1988. Somatomedin C and other hormones in dairy cows around parturition, in newborn calves and in milk. *J. Anim. Physiol. Anim. Nutr.*, **60**: 168-176. <https://doi.org/10.1111/j.1439-0396.1988.tb00190.x>
- Sellier, P., 2000. Genetically caused retarded growth in animals. *Domest. Anim. Endocrinol.*, **19**: 105-119. [https://doi.org/10.1016/S0739-7240\(00\)00071-0](https://doi.org/10.1016/S0739-7240(00)00071-0)
- Senaris, R., Garcia-Caballero, T.S., Casabiell, X.S., Gallego, R.A., Castro, R.N., Considine, R.V., Dieguez, C. and Casanueva, F.F., 1997. Synthesis of leptin in human placenta. *Endocrinology*, **138**: 4501-4504. <https://doi.org/10.1210/endo.138.10.5573>
- Shen, L., Zhu, Y., Xiao, J., Deng, J., Peng, G., Zuo, Z., Yu, S., Ma, X., Zhong, Z. and Ren, Z. 2019. Relationship of adiponectin, leptin, visfatin and IGF-1 in cow's venous blood and venous cord blood with calf birth weight. *Pol. J. Vet. Sci.*, **22**: 541-548.
- Sivan, E., Mazaki-Tovi, S., Pariente, C., Efraty, Y., Schiff, E., Hemi, R. and Kanety, H., 2003. Adiponectin in human cord blood: relation to fetal birth weight and gender. *J. clin. Endocrinol. Metab.*, **88**: 5656-5660. <https://doi.org/10.1210/jc.2003-031174>
- Vaughan, O.R. and Fowden, A.L., 2016. Placental metabolism: Substrate requirements and the response to stress. *Reprod. Domest. Anim.* **51**: 25-35. <https://doi.org/10.1111/rda.12797>
- Weyermann, M., Beermann, C., Brenner, H. and Rothenbacher, D., 2006. Adiponectin and leptin in maternal serum, cord blood, and breast milk. *Clin. Chem.*, **52**: 2095-2102. <https://doi.org/10.1373/clinchem.2006.071019>
- Wu, S., Hassan, F.U., Luo, Y., Fatima, I., Ahmed, I., Ihsan, A., Safdar, W., Liu, Q. and Rehman, S.U., 2021. Comparative genomic characterization of buffalo fibronectin type III domain proteins: Exploring the novel role of FNDC5/Irisin as a ligand of gonadal receptors. *Biology*, **10**: 1207. <https://doi.org/10.3390/biology10111207>
- Yoshimitsu, N., Douchi, T., Kamio, M. and Nagata, Y., 2000. Differences in umbilical venous and arterial leptin levels by mode of delivery. *Obstet. Gynecol.*, **96**: 342-345. <https://doi.org/10.1097/00006250-200009000-00005>
- Yoshimitsu, N., Douchi, T., Yamasaki, H., Nagata, Y., Andoh, T. and Hatano, H., 1999. Differences in umbilical cord serum lipid levels with mode of delivery. *Br. J. Obstet. Gynaecol.*, **106**: 144-147. <https://doi.org/10.1111/j.1471-0528.1999.tb08214.x>
- Yüksel, M.A., Öncül, M., Tüten, A., İmamoğlu, M., Açıkgöz, A.S., Kücür, M. and Madazlı, R., 2014. Maternal serum and fetal cord blood irisin levels in gestational diabetes mellitus. *Diab. Res. clin. Pract.*, **104**: 171-181. <https://doi.org/10.1016/j.diabres.2013.12.025>