GLUCOSE RELATED ENDOCRINE AND METABOLIC RESPONSES FOLLOWING BOLUS INTRAVENOUS HYPERTONIC DEXTROSE ADMINISTRATION IN IRANIAN FAT-TAILED EWES AT DIFFERENT PRE AND POST PARTURITION PERIODS

A. CHALMEH, A. MIRZAEI, M. POURJAFAR, K. BADIEI,
M. MAZROUEI SEBDANI, I. SAADAT AKHTAR & M. HADI ZAREI

Department of Clinical Sciences, School of Veterinary Medicine, Shiraz University,
Shiraz, Iran

Summary

Chalmeh, A., A. Mirzaei, M. Pourjafar, K. Badiei, M. Mazrouei Sebdani, I. Saadat Akhtar & M. Hadi Zarei, 2020. Glucose related endocrine and metabolic responses following bolus intravenous hypertonic dextrose administration in Iranian fat-tailed ewes at different pre and post parturition periods. *Bulg. J. Vet. Med.*, **23**, No 1, 44–59.

Providing glucose as primary metabolic fuel for maintenance, foetal growth and milk production may be considered necessary for protection against negative energy balance and metabolic disorders. Five adult Ghezel ewes were selected 4 weeks before their parturition and followed at 2 weeks before, 2 and 4 weeks and 2, 3 and 4 months after parturition. Dextrose 50% was administered at 500 mg/kg, 10 mL/kg/hour, and blood samples were collected from all ewes prior to and 1, 2, 3 and 4 hours after 50% dextrose infusion. Serum levels of glucose, beta-hydroxybutyric acid, non-esterified fatty acids, cholesterol, triglyceride, high, low and very low density lipoproteins, insulin, triiodothyronine, thyroxine, prolactin, cortisol and insulin like growth factor-1 were evaluated. Glucose and insulin were increased significantly and immediately following intravenous dextrose administration at all studied periods. The levels of beta-hydroxybutyric acid and non-esterified fatty acids were significantly decreased following dextrose infusion at all periods. Triiodothyronine was decreased in pregnant ewes and increased in non-pregnant, lactating ones. The significant increasing cortisol patterns were detected at 2 and 4 weeks before and 2 and 4 weeks after parturition following dextrose administrations. The decreasing patterns of insulin like growth factor-1 were seen in all studied periods. Prolactin was significantly increased following dextrose administration at 4 and 2 weeks before and 2 weeks after parturition. Bolus intravenous hypertonic dextrose administration could induce the obvious endocrine and metabolic responses in Ghezel ewes via providing a source of energy and the glucose is an important direct controller of metabolic interactions in Ghezel ewes.

Key words: Ghezel ewe, lactogenesis, metabolism, parturition, pregnancy

INTRODUCTION

Ghezel is an indigenous Iranian fat-tailed, medium-sized dairy sheep breed commonly distributed in the Fars province, southwest Iran. It is reared under semiarid conditions and the physiological importance of the fat tail is to provide energy during drought seasons and feed deprivation situations which are not uncommon in Iran. The peri-parturient period is critical for both animal health and performance (Mavrogianni & Brozos, 2008) and like other breeds, Ghezel ewes are susceptible to serious metabolic diseases due to high producing performances and are at high risk for negative energy balance (Morgante, 2004).

Pregnancy and parturition are accompanied by endocrine changes that exceed those occurring in time. Concurrent with shifts in endocrine profile are metabolic changes that facilitate diversion of nutrients away from maternal stores toward foetus during pregnancy and milk synthesis and nurturing of the newborn after parturition. During pregnancy and lactation, all metabolic pathways are involved in sustaining foetal growth and lactogenesis, respectively (Bell *et al.*, 2000). In ruminants, the massive energy demand is partly provided through gluconeogenesis and glucose has a central role in metabolism and homeostatic control (Herdt, 2000).

The identification of changes in the metabolism of ewes in various reproduction phases, the determination of abnormal metabolic states, and the prediction of some metabolic disorders, could provide some advantages to producers (Balikci *et al.*, 2007). Several studies on factors associated with the marked metabolic changes in humans, laboratory animals (Connolly *et al.*, 2004) and dairy cows (Chalmeh *et al.*, 2015) indicated that the peri-par-

turition period is probably accompanied by distinct hormonal and metabolic changes that modify homeorhetic adaptations of the whole body. The periods of pregnancy and lactation induce a huge metabolic challenge and the metabolic profiles can be used as important criteria to evaluate the health status (Hawagane *et al.*, 2009). Substantial body condition score losses occur due to negative energy balance after parturition which is indicated by alterations in blood metabolic and hormone profiles (Wathes *et al.*, 2009). Ruminants require high level of glucose or its precursors for milk production and maintaining reproductive performance. The blood glucose concentration in ewes could be different (Firat & Ozpinar, 1996), depending on various physiological conditions and the level of production as well as in various stages of some metabolic diseases. In the absence of glucose, ketone bodies and urea concentrations produced from fat and protein catabolism increase from normal condition up to different physiological and pathological conditions (Van Saun, 2000).

Administration of glucose as the primary metabolic fuel for maintenance, foetal growth and milk production is suggested as a necessary part of protection against negative energy balance and metabolic disorders in sheep during pre and post parturition periods. There are several studies on endocrine and metabolic responses of high producing Holstein dairy cows to glucose administration based on the stage of lactation (De Koster & Opsomer, 2013; Chalmeh *et al.*, 2015) but to our knowledge, there are no data on the variations of energy-related metabolites around parturition following intravenous glucose administration in Ghezel ewes. Furthermore, appropriate informa-

tion about the baseline values of circulating endocrine and metabolic profile for prevention and control of many production diseases in sheep is necessary and would be useful index for distinction of the physiological appearance in pregnant and non-pregnant ewes.

MATERIALS AND METHODS

Animals

The present study was carried out in the winter of 2015 with 5 adult Ghezel ewes at a farm around Shiraz, Southwest of Iran (latitude 29° 44' N; longitude of 52° 37' E, 1810 m above sea level). Ewes were housed in open-shed barns with free access to water and shade. Ration included alfalfa hay, corn silage, wheat straw, barley grain, wheat bran, cottonseed meal, urea, calcium carbonate, common salt (NaCl) and vitamin-mineral premix. All animals were clinically healthy, had no history of debilitating disease and were free from internal and external parasites due to routine antiparasitic programmes at the farm. Body condition score (BCS) was estimated based on 0–5 system and pregnancy was diagnosed using a real-time ultrasound scanner equipped with a 3.5 MHz sectorial convex probe (CTS-900V, SIUI, China). The ewes were examined transabdominally in standing position. The sheep were selected at 4 weeks before parturition and followed at 2 weeks before, 2 and 4 weeks and 2, 3 and 4 months after parturition.

Bolus intravenous glucose administration

All experiments were done one hour after morning meal, at 06:00 AM, approximately. A 16-gauge 5.1-cm catheter was secured in the right jugular vein and used for blood samplings and dextrose infu-

sions. A blood sample was taken immediately after catheterisation, and dextrose 50% (Zoopha®, Parnian Co., Iran) was subsequently administered at 500 mg/kg, 10 mL/kg/hour, (De Koster & Opsomer, 2013). Blood samples were collected from all ewes through the fixed catheter prior to and 1, 2, 3 and 4 hours after dextrose 50% infusion in plain tubes.

Serum hormonal and metabolic biomarker analyses

Immediately after blood collections, sera were separated by centrifugation for 10 min at 3,000×g and stored at –22 °C until assayed. Glucose was assayed by an enzymatic (glucose oxidase) colorimetric method (ZistChems®, Tehran, Iran). Beta-hydroxybutyric acid (BHBA) and non-esterified fatty acids (NEFA) were assayed by colorimetric method (Ranbut®, Ireland). The sera were analyzed for cholesterol by a modified Abell-Kendall/Levy-Brodie (A-K) method (Abbel *et al.*, 1952; Burtis & Ashwood, 1994), triglyceride (TG) by the enzymatic procedure of McGowan *et al.* (1983). High, low and very low density lipoproteins (HDL, LDL and VLDL) were analysed by suggested methods (Friedewald *et al.*, 1972; Burtis & Ashwood, 1994). Insulin was measured by ovine insulin ELISA kit (Cusabio®, China, specificity 100%, intra-assay and inter-assay CV < 8% and 10%, respectively). Serum triiodothyronine (T3) concentrations were determined using a competitive enzyme immunoassay kit (Padtan Elm Co., Tehran, Iran). The intra- and inter-assay CVs of the assays were 12.6% and 13.2%, respectively. The sensitivity of the test was 0.2 ng/mL. Serum thyroxine (T4) concentrations were measured using a competitive enzyme immunoassay kit (Monobind Inc., CA, USA). The intra- and inter-assay CVs of the assays were

3.0% and 3.7%, respectively. The sensitivity of the test was 0.4 mg/dL. Prolactin was measured by competitive enzyme immunoassay technique using commercial ovine prolactin ELISA Kit (Wuhan Huamei Cusabio Biotech Co., Ltd, China). Serum cortisol concentrations were determined by enzyme immunoassay colorimetric method (AccuBind® ELISA kit; Monobind Inc., CA, USA) with sensitivity of 0.25 µg/dL. Serum levels of insulin like growth factor-1 (IGF-1) were evaluated by ELISA kit (ImmunoDiagnostic Systems®) with sensitivity equal to 3.1 µg/L.

Statistical analyses

All data are presented as median (min-max). Differences among the average concentrations of each parameter at similar hours in the different experimental groups were analysed by Kruskal-Wallis test. Spearman's correlation test was also used to evaluate the relationships among glucose and other circulating parameters at different pre and post partum periods of Ghezel ewes. Statistical analyses were performed by using SPSS software (SPSS for Windows, version 20, SPSS Inc, Chicago, IL, USA). The level of significance was set at $P < 0.05$.

RESULTS

Baseline levels of circulating endocrine and metabolic biomarkers at different pre and post partum periods of Iranian fat-tailed ewes are presented in Tables 1 to 3 at hour 0. Glucose related endocrine and metabolic responses following bolus intravenous hypertonic dextrose administration at different pre and post parturition periods of Ghezel ewes are also shown in Tables 1 to 3.

In all experimental groups glucose increased significantly and immediately

following bolus intravenous dextrose 50% administration at all studied periods ($P < 0.05$; Table 1). Its concentration decreased subsequently and reached baseline values at hour 4. Significant increases of insulin levels were seen in all studied groups from zero to 1st hour after dextrose administration. In pre parturition periods, insulin levels at hour 4 remained significantly higher than baseline values ($P < 0.05$; Table 1); but the serum insulin levels in remaining groups decreased near to baseline levels at 4th hour. At this hour, insulin levels at 4 weeks before parturition period were significantly higher vs 2 weeks before parturition and insulin levels in both were significantly higher compared to other studied periods ($P < 0.05$).

Circulating levels of BHBA and NEFA at hour zero in 4 weeks before parturition were higher than other studied periods (Table 1). Their values were significantly decreased following bolus intravenous hypertonic dextrose administration at different pre and post parturition periods of studied Ghezel ewes. BHBA and NEFA at 4th hour were significantly lower than their baseline level at hour zero in all studied periods; furthermore, the lowest BHBA and NEFA concentrations were detected 4 hours after dextrose administration, at postpartum month 4 ($P < 0.05$).

The lowest levels of TG and cholesterol were measured 4 months after parturition ($P < 0.05$; Table 2). Serum concentrations of TG were significantly decreased after dextrose 50% administrations from hour zero to hour 1 in all studied periods but remained without significant alterations after the 1st hour. There were no significant changing patterns of cholesterol after hypertonic dextrose administration in all periods ($P > 0.05$). Circulating cholesterol concentrations before

Table 1. Circulating levels of glucose, insulin, BHBA and NEFA [median (min-max); n=5] following bolus intravenous hypertonic dextrose administration (dextrose 50%; 500 mg/kg, 10 mL/kg/hour) at different pre (PP) and post partum (AP) periods of Chezel ewes

Periods	0 h	1 h	2 h	3 h	4 h
Glucose (mmol/L)					
4 weeks PP	3.44 (3.44-3.50) ^a	19.47 (15.18-19.47) ^a	12.59 (10.17-12.59) ^a	8.25 (6.82-8.25) ^a	4.51 (4.51-4.73) ^a
2 weeks PP	5.00 (4.5-5.0) ^a	16.90 (15.9-16.9) ^a	17.80 (17.8-17.8) ^a	7.30 (7.3-9.6) ^a	4.20 (4.2-6.1) ^a
2 weeks AP	4.29 (3.57-4.29) ^a	17.21 (11.99-17.21) ^a	16.39 (9.73-16.39) ^a	6.54 (6.54-7.26) ^a	4.18 (3.90-4.18) ^a
4 weeks AP	3.63 (3.63-3.63) ^a	17.93 (17.10-17.93) ^a	10.28 (10.28-11.71) ^a	5.22 (5.22-8.47) ^a	3.90 (3.90-6.38) ^a
2 months AP	4.29 (4.07-4.29) ^a	16.55 (16.50-16.55) ^a	9.02 (9.02-10.83) ^a	6.93 (6.93-7.26) ^a	4.62 (4.62-4.95) ^a
3 months AP	4.45 (3.08-4.45) ^a	12.87 (12.87-15.29) ^a	7.09 (7.09-10.56) ^a	4.67 (4.67-7.09) ^a	4.45 (4.45-5.17) ^a
4 months AP	2.20 (2.20-3.85) ^a	16.88 (15.01-16.88) ^a	8.14 (8.14-10.34) ^a	3.63 (3.63-8.80) ^a	2.80 (2.80-5.22) ^a
Insulin (μU/mL)					
4 weeks PP	56 (56-110) ^b	96 (76-148) ^b	88 (87-158) ^a	106 (82-110) ^a	85 (57-152) ^a
2 weeks PP	75 (68-75) ^b	90 (84-113) ^c	106 (54-126) ^c	113 (42-113) ^b	106 (83-153) ^b
2 weeks AP	70 (59-70) ^c	111 (109-161) ^a	111 (106-111) ^b	75 (49-89) ^c	85 (69-116) ^c
4 weeks AP	139 (139-139) ^b	96 (53-111) ^c	98 (64-113) ^c	106 (103-125) ^a	92 (92-106) ^c
2 months AP	151 (103-151) ^b	84 (63-179) ^b	75 (70-75) ^b	128 (88-128) ^a	89 (75-92) ^c
3 months AP	120 (120-179) ^b	106 (102-139) ^b	98 (84-148) ^c	62 (62-77) ^b	92 (85-136) ^c
4 months AP	186 (123-186) ^a	113 (105-119) ^b	153 (89-153) ^a	77 (63-120) ^b	91 (56-112) ^c
BHBA (mmol/L)					
4 weeks PP	0.12 (0.11-0.12) ^a	0.13 (0.08-0.14) ^a	0.07 (0.05-0.07) ^a	0.09 (0.07-0.11) ^c	0.09 (0.08-0.10) ^b
2 weeks PP	0.09 (0.07-0.09) ^b	0.06 (0.06-0.07) ^c	0.07 (0.06-0.12) ^c	0.10 (0.05-0.10) ^b	0.09 (0.06-0.13) ^a
2 weeks AP	0.08 (0.08-0.14) ^a	0.09 (0.09-0.11) ^b	0.08 (0.07-0.08) ^b	0.09 (0.08-0.11) ^b	0.13 (0.07-0.15) ^a
4 weeks AP	0.08 (0.08-0.08) ^b	0.07 (0.06-0.11) ^c	0.06 (0.04-0.09) ^c	0.09 (0.06-0.10) ^a	0.08 (0.08-0.09) ^a
2 months AP	0.06 (0.06-0.12) ^b	0.08 (0.05-0.11) ^c	0.09 (0.09-0.10) ^c	0.07 (0.07-0.12) ^a	0.07 (0.06-0.11) ^a
3 months AP	0.11 (0.10-0.13) ^a	0.10 (0.05-0.10) ^b	0.07 (0.06-0.09) ^b	0.09 (0.07-0.09) ^b	0.07 (0.06-0.09) ^a
4 months AP	0.11 (0.10-0.11) ^a	0.08 (0.06-0.13) ^b	0.08 (0.08-0.15) ^b	0.08 (0.05-0.09) ^b	0.07 (0.03-0.09) ^b
NEFA (mmol/L)					
4 weeks PP	92 (92-132) ^a	135 (122-168) ^a	88 (88-146) ^a	123 (114-162) ^a	172 (144-176) ^a
2 weeks PP	117 (98-117) ^b	102 (94-108) ^b	127 (120-142) ^a	108 (108-155) ^a	115 (94-148) ^a
2 weeks AP	108 (108-172) ^a	115 (114-160) ^a	94 (94-155) ^b	112 (82-128) ^a	152 (127-189) ^a
4 weeks AP	98 (98-98) ^b	89 (84-121) ^a	134 (79-142) ^a	134 (118-142) ^a	94 (94-103) ^c
2 months AP	128 (128-174) ^a	131 (127-196) ^b	119 (119-150) ^a	147 (142-147) ^a	116 (109-118) ^a
3 months AP	154 (120-162) ^a	134 (120-143) ^b	127 (124-155) ^c	142 (132-142) ^b	119 (115-134) ^a
4 months AP	116 (116-174) ^a	135 (121-190) ^b	88 (88-214) ^a	96 (93-162) ^a	108 (51-109) ^d

Different letters indicate significant differences among different periods at similar hours for each parameter (P<0.05).

Table 2. Circulating levels of TG, cholesterol, HDL, LDL and VLDL [median (min-max); n=5] following bolus intravenous hypertonic dextrose administration (dextrose 50%; 500 mg/kg, 10 mL/Kg/hour) at different pre (PP) and post partum (AP) periods of Ghezel ewes

Periods	0 h	1 h	2 h	3 h	4 h
TG (mmol/L)					
4 weeks PP	0.34 (0.18-0.34) ^a	0.13 (0.13-0.19) ^a	0.21 (0.21-0.25) ^a	0.19 (0.19-0.28) ^a	0.24 (0.08-0.24) ^a
2 weeks PP	0.24 (0.24-0.29) ^a	0.11 (0.11-0.29) ^a	0.20 (0.20-0.20) ^a	0.34 (0.34-0.46) ^a	0.19 (0.19-0.21) ^a
2 weeks AP	0.20 (0.20-0.20) ^b	0.17 (0.17-0.25) ^a	0.19 (0.18-0.19) ^a	0.13 (0.13-0.19) ^a	0.20 (0.20-0.28) ^a
4 weeks AP	0.33 (0.33-0.33) ^a	0.16 (0.16-0.19) ^a	0.21 (0.16-0.21) ^a	0.14 (0.14-0.20) ^a	0.19 (0.18-0.19) ^a
2 months AP	0.35 (0.20-0.35) ^a	0.19 (0.18-0.19) ^a	0.21 (0.21-0.21) ^a	0.21 (0.19-0.21) ^a	0.18 (0.18-0.18) ^a
3 months AP	0.21 (0.21-0.29) ^a	0.16 (0.16-0.19) ^a	0.17 (0.17-0.20) ^a	0.20 (0.11-0.20) ^a	0.18 (0.17-0.18) ^a
4 months AP	0.19 (0.19-0.19) ^b	0.21 (0.20-0.21) ^a	0.11 (0.11-0.21) ^a	0.17 (0.17-0.18) ^a	0.13 (0.13-0.18) ^a
Cholesterol (mmol/L)					
4 weeks PP	1.75 (1.31-1.75) ^a	1.62 (1.59-1.62) ^a	1.46 (1.46-1.67) ^a	1.72 (1.64-1.72) ^a	1.36 (1.36-1.57) ^a
2 weeks PP	1.62 (1.52-1.62) ^a	1.52 (1.46-1.52) ^a	1.49 (1.49-1.49) ^a	1.44 (1.41-1.44) ^a	1.18 (1.18-1.36) ^b
2 weeks AP	1.82 (1.36-1.82) ^a	1.26 (1.26-1.59) ^a	1.44 (1.44-1.82) ^a	1.15 (1.15-1.49) ^a	1.44 (1.44-1.57) ^b
4 weeks AP	1.88 (1.88-1.88) ^a	1.08 (1.08-1.49) ^b	1.77 (1.23-1.77) ^a	1.57 (1.57-1.57) ^a	1.80 (1.67-1.80) ^a
2 months AP	2.16 (1.44-2.16) ^b	2.29 (1.34-2.29) ^b	1.44 (1.44-1.57) ^b	1.82 (1.70-1.82) ^a	1.44 (1.00-1.44) ^a
3 months AP	1.08 (1.08-1.95) ^a	1.98 (1.70-1.98) ^b	1.88 (1.52-1.88) ^b	1.44 (0.97-1.44) ^b	1.26 (1.26-1.26) ^a
4 months AP	1.00 (1.00-1.82) ^c	1.21 (1.21-1.44) ^c	1.57 (1.39-1.57) ^c	1.44 (1.41-1.44) ^b	1.00 (1.00-1.41) ^b

Different letters indicate significant differences among different periods at similar hours for each parameter (P<0.05).

Table 2 (cont'd). Circulating levels of TG, cholesterol, HDL, LDL and VLDL [median (min-max); n=5] following bolus intravenous hypertonic dextrose administration (dextrose 50%; 500 mg/kg, 10 mL/Kg/hour) at different pre (PP) and post partum (AP) periods of Ghezel ewes

Periods	0 h	1 h	2 h	3 h	4 h
HDL (mmol/L)					
4 weeks PP	0.03 (0.03-0.03) ^a	0.03 (0.03-0.03) ^a	0.03 (0.03-0.03) ^a	0.03 (0.03-0.03) ^a	0.03 (0.03-0.03) ^a
2 weeks PP	0.02 (0.02-0.02) ^b	0.03 (0.03-0.03) ^b	0.02 (0.02-0.02) ^b	0.03 (0.03-0.03) ^b	0.03 (0.03-0.03) ^a
2 weeks AP	0.02 (0.02-0.03) ^c	0.03 (0.03-0.03) ^b	0.03 (0.02-0.03) ^c	0.03 (0.03-0.03) ^c	0.03 (0.03-0.03) ^c
4 weeks AP	0.03 (0.03-0.03) ^b	0.03 (0.02-0.03) ^c	0.03 (0.03-0.03) ^a	0.03 (0.03-0.03) ^c	0.03 (0.02-0.03) ^c
2 months AP	0.02 (0.02-0.02) ^c	0.03 (0.03-0.03) ^b	0.03 (0.03-0.03) ^b	0.03 (0.03-0.03) ^c	0.03 (0.03-0.03) ^b
3 months AP	0.02 (0.02-0.02) ^c	0.02 (0.02-0.02) ^c	0.03 (0.03-0.03) ^b	0.03 (0.03-0.03) ^c	0.03 (0.02-0.03) ^a
4 months AP	0.03 (0.02-0.03) ^b	0.03 (0.02-0.03) ^c	0.03 (0.03-0.03) ^b	0.03 (0.03-0.03) ^b	0.02 (0.02-0.03) ^c
LDL (mmol/L)					
4 weeks PP	1.56 (1.20-1.56) ^a	1.53 (1.47-1.53) ^a	1.34 (1.34-1.53) ^a	1.60 (1.48-1.60) ^a	1.22 (1.22-1.50) ^a
2 weeks PP	1.49 (1.36-1.49) ^a	1.44 (1.30-1.44) ^a	1.37 (1.37-1.37) ^a	1.26 (1.17-1.26) ^b	1.06 (1.06-1.24) ^b
2 weeks AP	1.71 (1.24-1.71) ^a	1.15 (1.15-1.45) ^c	1.32 (1.32-1.72) ^a	1.06 (1.06-1.37) ^c	1.32 (1.32-1.41) ^a
4 weeks AP	1.70 (1.70-1.70) ^b	0.98 (0.98-1.38) ^b	1.65 (1.13-1.65) ^b	1.47 (1.44-1.47) ^b	1.68 (1.56-1.68) ^c
2 months AP	1.98 (1.32-1.98) ^b	2.18 (1.22-2.18) ^b	1.31 (1.31-1.44) ^a	1.70 (1.57-1.70) ^a	1.33 (0.89-1.33) ^a
3 months AP	0.95 (0.95-1.80) ^b	1.88 (1.58-1.88) ^b	1.77 (1.40-1.77) ^b	1.31 (0.89-1.31) ^b	1.14 (1.14-1.16) ^a
4 months AP	0.88 (0.88-1.71) ^a	1.08 (1.08-1.32) ^a	1.49 (1.26-1.49) ^b	1.33 (1.30-1.33) ^b	0.91 (0.91-1.30) ^b
VLDL (mmol/L)					
4 weeks PP	0.15 (0.08-0.15) ^a	0.06 (0.06-0.08) ^a	0.09 (0.09-0.11) ^a	0.08 (0.08-0.13) ^a	0.11 (0.03-0.11) ^a
2 weeks PP	0.11 (0.11-0.13) ^a	0.05 (0.05-0.13) ^a	0.09 (0.09-0.09) ^a	0.15 (0.15-0.21) ^a	0.08 (0.08-0.09) ^a
2 weeks AP	0.09 (0.09-0.09) ^b	0.07 (0.07-0.11) ^a	0.08 (0.08-0.08) ^a	0.06 (0.06-0.08) ^a	0.09 (0.09-0.13) ^a
4 weeks AP	0.15 (0.15-0.15) ^a	0.07 (0.07-0.08) ^a	0.09 (0.07-0.09) ^a	0.06 (0.06-0.09) ^a	0.08 (0.08-0.08) ^a
2 months AP	0.16 (0.09-0.16) ^a	0.08 (0.08-0.08) ^a	0.09 (0.09-0.09) ^a	0.09 (0.08-0.09) ^a	0.08 (0.08-0.08) ^a
3 months AP	0.09 (0.09-0.13) ^a	0.07 (0.07-0.08) ^a	0.07 (0.07-0.09) ^a	0.09 (0.05-0.09) ^a	0.08 (0.07-0.08) ^a
4 months AP	0.08 (0.08-0.08) ^b	0.09 (0.09-0.09) ^a	0.05 (0.05-0.09) ^a	0.07 (0.07-0.08) ^a	0.06 (0.06-0.08) ^a

Different letters indicate significant differences among different periods at similar hours for each parameter (P<0.05).

and after intravenous dextrose infusions 4 months after parturition were significantly lower than during other studied periods ($P<0.05$).

HDL levels in all studied periods were increased significantly following hypertonic dextrose administrations ($P<0.05$; Table 2). In all periods, HDL at hour 4 was significantly higher than its baseline levels at hour zero. There were significant decreasing patterns of LDL in all studied groups following bolus intravenous dextrose infusions ($P<0.05$; Table 2). In all periods, LDL at hour 4 was significantly lower than its baseline levels at hour zero. The lowest concentrations of VLDL were detected 4 months after parturition ($P<0.05$; Table 2). VLDL were significantly decreased after dextrose administrations from hour zero to hour 1 in all studied periods but remained without significant alterations after 1st hour (Table 2).

Two months after parturition serum T3 and T4 levels were significantly higher compared to other studied periods at hour zero (Table 3). There were significantly decreasing T3 patterns before parturition ($P<0.05$) but its values were significantly increased ($P<0.05$) in remaining groups following dextrose administration (Table 3). By the 4th hour, the lowest levels of T3 were detected in 2 and 4 weeks before parturition groups ($P<0.05$). Before and after dextrose administrations, circulating T4 concentrations 2 and 4 months after parturition were significantly higher than other groups ($P<0.05$; Table 3). There were no significant changing patterns of T4 after hypertonic dextrose administration in all experimental periods ($P>0.05$; Table 3).

The lowest baseline levels of cortisol were detected 2 weeks before and 2 and 4 weeks after parturition in comparison with other periods ($P<0.05$; Table 3). Cortisol

increased significantly 2 and 4 weeks before and 2 and 4 weeks after parturition following bolus intravenous dextrose 50% administrations and in the remaining periods, showed significant decrease ($P<0.05$; Table 3). Before and after intravenous dextrose administrations, IGF-1 was significantly higher than other experimental groups 4 weeks before parturition ($P<0.05$; Table 3). In all studied periods, the significant decreasing patterns of this hormone were detected following dextrose administrations. The lowest baseline levels of prolactin were detected 2 weeks before and 2 weeks after parturition in comparison to other ones, but its baseline value at 3 months after parturition was significantly higher than other periods ($P<0.05$; Table 3). The significantly increasing patterns of prolactin were seen after dextrose administrations 2 and 4 weeks before and 2 weeks after parturition; however, prolactin levels were significantly decreased in remaining periods after bolus intravenous dextrose 50% infusion ($P<0.05$; Table 3).

The relationships among circulating glucose and other studied parameters in Ghezel ewes at different pre and post partum periods are presented in Table 4. Glucose had negative and significant correlation with insulin, BHBA and NEFA in all studied periods ($P<0.05$). Its relationships with cortisol were positive and significant in all periods. The correlations among glucose and lipid profile were negative and non-significant during the study ($P>0.05$; Table 4) while its relationships with other evaluated hormones were positive and non-significant.

DISCUSSION

Ruminants are well adapted to satisfy their energy needs from volatile fatty acids ab-

Table 3. Circulating levels of cortisol, IGF-1, prolactin, T3 and T4 [median (min-max); n=5] following bolus intravenous hypertonic dextrose administration (dextrose 50%; 500 mg/kg, 10 mL/kg/hour) at different pre (PP) and post partum (AP) periods of Ghezel ewes

Periods	0 h	1 h	2 h	3 h	4 h
Cortisol (nmol/L)					
4 weeks PP	652 (652-665) ^a	740 (693-954) ^a	465 (465-990) ^a	550 (536-113) ^a	803 (739-1091) ^a
2 weeks PP	652 (652-665) ^a	740 (693-954) ^a	465 (465-990) ^a	550 (536-113) ^a	803 (740-1091) ^a
2 weeks AP	110 (110-137) ^b	602 (140-891) ^a	344 (344-784) ^b	646 (399-946) ^b	918 (665-1452) ^b
4 weeks AP	517 (517-517) ^c	382 (129-490) ^b	539 (349-577) ^c	613 (349-723) ^b	530 (421-531) ^c
2 months AP	401 (401-1053) ^c	624 (330-1358) ^a	418 (418-503) ^a	514 (514-778) ^a	432 (283-473) ^d
3 months AP	781 (583-1031) ^d	583 (388-740) ^c	679 (558-696) ^d	542 (393-541) ^a	558 (421-756) ^c
4 months AP	586 (586-1980) ^c	561 (492-1122) ^c	401 (401-1257) ^a	500 (308-863) ^a	385 (52-514) ^d
IGF-1 (nmol/L)					
4 weeks PP	16.2 (14.6-16.2) ^a	16.7 (12.8-17.5) ^a	16.2 (15.4-16.2) ^a	20.6 (10.7-20.8) ^a	17.1 (12.8-18.3) ^a
2 weeks PP	9.1 (9.1-9.5) ^b	6.2 (6.2-17.5) ^b	12.5 (7.7-21.2) ^b	4.1 (4.1-14.6) ^c	11.2 (6.4-17.5) ^b
2 weeks AP	9.8 (9.8-12.8) ^b	9.6 (8.9-18.5) ^b	4.4 (4.4-22.5) ^c	11.2 (6.4-15.1) ^b	15.9 (15.3-24.3) ^a
4 weeks AP	9.6 (9.6-9.6) ^b	8.5 (7.7-16.6) ^b	10.4 (9.6-14.6) ^d	16.2 (14.2-17.2) ^b	11.9 (11.1-11.9) ^b
2 months AP	11.2 (11.2-20.6) ^c	12.6 (9.6-22.7) ^c	10.7 (10.7-13.8) ^d	9.1 (9.1-16.7) ^d	8.6 (7.7-12.0) ^c
3 months AP	14.6 (12.3-17.5) ^a	12.3 (5.7-20.2) ^c	13.7 (11.2-13.8) ^b	9.1 (9.1-10.9) ^d	12.6 (7.5-16.6) ^b
4 months AP	10.3 (10.3-12.5) ^c	12.5 (8.6-17.5) ^c	7.7 (7.7-20.6) ^c	7.4 (5.4-14.6) ^d	5.3 (2.3-11.2) ^c
Prolactin (µg/L)					
4 weeks PP	96 (96-194) ^a	214 (174-227) ^a	98 (98-176) ^a	124 (76-190) ^a	166 (155-276) ^a
2 weeks PP	72 (72-85) ^b	64 (62-109) ^b	122 (49-145) ^b	58 (58-148) ^b	86 (76-115) ^b
2 weeks AP	63 (63-219) ^b	125 (55-176) ^a	80 (80-109) ^a	97 (74-145) ^c	149 (96-296) ^a
4 weeks AP	83 (83-83) ^b	97 (94-106) ^c	98 (55-125) ^a	120 (76-145) ^a	66 (66-74) ^c
2 months AP	75 (75-197) ^b	129 (109-259) ^a	122 (108-122) ^b	83 (83-161) ^c	74 (62-94) ^b
3 months AP	159 (112-276) ^c	159 (122-176) ^a	147 (132-173) ^b	107 (91-107) ^a	96 (82-97) ^b
4 months AP	86 (86-317) ^b	98 (74-255) ^c	70 (70-194) ^c	109 (52-266) ^a	65 (40-115) ^c

Different letters indicate significant differences among different periods at similar hours for each parameter (P<0.05).

Table 3 (cont'd). Circulating levels of cortisol, IGF-1, prolactin, T3 and T4 [median (min-max); n=5] following bolus intravenous hypertonic dextrose administration (dextrose 50%; 500 mg/kg, 10 mL/Kg/hour) at different pre (PP) and post partum (AP) periods of Ghezel ewes

Periods	0 h	1 h	2 h	3 h	4 h
T3 (nmol/L)					
4 weeks PP	1.75 (1.75-2.20) ^a	1.97 (1.85-2.29) ^a	1.65 (1.65-2.00) ^a	1.63 (1.55-2.04) ^a	1.43 (1.39-2.17) ^a
2 weeks PP	2.11 (1.78-2.11) ^b	2.00 (1.80-2.21) ^a	2.04 (1.94-2.18) ^b	1.83 (1.68-1.83) ^a	1.63 (1.40-2.00) ^a
2 weeks AP	1.69 (1.69-1.97) ^a	1.80 (1.51-2.33) ^a	2.09 (2.09-2.15) ^b	2.33 (1.66-2.37) ^b	2.01 (1.55-2.47) ^b
4 weeks AP	1.74 (1.74-1.74) ^a	1.81 (1.72-1.86) ^a	1.83 (1.65-1.85) ^a	1.66 (1.66-2.07) ^a	1.66 (1.39-1.80) ^a
2 months AP	1.81 (1.81-2.41) ^a	2.26 (2.20-2.53) ^b	2.21 (2.07-2.21) ^b	2.30 (2.20-2.30) ^b	2.01 (1.92-2.20) ^b
3 months AP	1.40 (1.40-1.78) ^a	2.15 (2.03-2.37) ^b	1.95 (1.68-1.95) ^a	1.55 (1.55-1.95) ^a	1.94 (1.45-2.14) ^b
4 months AP	1.74 (1.74-2.30) ^a	1.94 (1.88-2.96) ^a	2.01 (2.01-2.49) ^b	2.23 (1.68-2.43) ^b	2.07 (1.81-2.20) ^b
T4 (nmol/L)					
4 weeks PP	61.1 (61.1-85.5) ^a	76.1 (53.2-100.5) ^a	57.5 (57.5-73.2) ^a	87.2 (56.2-91.5) ^a	82.6 (54.8-87.7) ^a
2 weeks PP	86.7 (66.1-86.7) ^b	63.8 (58.8-84.4) ^b	65.2 (60.2-96.1) ^a	60.6 (60.6-74.2) ^b	62.9 (60.7-82.7) ^b
2 weeks AP	67.5 (59.8-67.5) ^a	61.2 (45.6-67.8) ^b	77.7 (60.8-77.7) ^c	74.7 (45.9-84.4) ^b	62.6 (43.7-89.4) ^b
4 weeks AP	63.7 (63.7-63.7) ^a	59.7 (44.4-73.1) ^b	69.2 (41.3-71.8) ^b	84.2 (67.1-84.2) ^a	64.6 (46.5-83.1) ^b
2 months AP	80.9 (80.9-104.2) ^b	82.2 (57.1-91.5) ^a	88.1 (86.3-88.1) ^c	88.2 (88.2-107.5) ^a	95.7 (57.6-100.2) ^a
3 months AP	75.1 (75.1-75.4) ^a	88.4 (69.7-88.8) ^a	63.5 (48.7-80.4) ^c	71.2 (71.2-106.9) ^b	75.4 (60.8-91.5) ^b
4 months AP	84.2 (84.2-114.1) ^b	84.8 (58.8-111.3) ^a	85.7 (85.7-117.1) ^c	100.9 (57.5-111.3) ^c	102.1 (73.6-122.9) ^c

Different letters indicate significant differences among different periods at similar hours for each parameter (P<0.05).

Table 4. Correlations among circulating glucose and other studied parameters at different pre and post partum periods of Ghezel ewes. The asterisk indicates a significant relationship ($P < 0.05$)

Parameters	4 weeks before parturition	2 weeks before parturition	2 weeks after parturition	4 weeks after parturition	2 months after parturition	3 months after parturition	4 months after parturition
BHBA	-0.721*	-0.649*	-0.511*	-0.629*	-0.732*	-0.812*	-0.778*
NEFA	-0.642*	-0.527*	-0.612*	-0.791*	-0.799*	-0.859*	-0.729*
TG	-0.118	-0.214	-0.370	-0.421	-0.319	-0.301	-0.314
Cholesterol	-0.355	-0.208	-0.372	-0.332	-0.318	-0.299	-0.301
HDL	-0.329	-0.370	-0.298	-0.287	-0.299	-0.318	-0.412
LDL	-0.482	-0.397	-0.279	-0.311	-0.328	-0.381	-0.425
VLDL	-0.355	-0.381	-0.231	-0.289	-0.278	-0.411	-0.389
Insulin	-0.622*	-0.711*	-0.851*	-0.742*	-0.821*	-0.910*	-0.921*
Cortisol	0.581*	0.637*	0.722*	0.838*	0.760*	0.811*	0.878*
IGF-I	0.320	0.428	0.429	0.399	0.314	0.229	0.274
Prolactin	0.212	0.308	0.311	0.340	0.320	0.422	0.436
T3	0.204	0.297	0.328	0.333	0.371	0.412	0.384
T4	0.314	0.361	0.319	0.340	0.438	0.400	0.335

sorbed from gastrointestinal tract and converted to glucose via hepatic gluconeogenesis (Kaneko *et al.*, 2008). In these animals, volatile fatty acids are the major energy source rather than direct sources of glucose. Thus, insulin plays a slightly different role in ruminants vs. non-ruminants, though many aspects of insulin metabolism are the same (De Koster & Opsomer, 2013). Energy demands could be also provided from direct glucose administration in the bloodstream. Bolus intravenous hypertonic dextrose administration or intravenous glucose tolerance test is used to detect insulin resistant ruminants (De Koster & Opsomer, 2013). In insulin resistant animals, serum concentrations of insulin and glucose are high after dextrose administration. Based on the other reports, insulin resistance in dairy cows may be detectable at post parturition periods, characterised with negative energy balance (Chalmeh *et al.*, 2015), but the results of the present research showed that at pre parturition periods, Ghezel ewes had high levels of insulin and glucose at 4th hour after bolus intravenous hypertonic dextrose administration (Table 1); hence, it may be suggested that pregnant ewes probably showed insulin resistance in comparison with non-pregnant ones.

A number of investigators showed that ewes in late gestation exhibited higher blood ketone body concentrations, higher entry rates of ketone bodies, and lower blood glucose (Harmeyer & Schlumbohm, 2006) than non-gestating sheep. A reduced disposal rate of BHBA during late gestation in association with a high rate of hepatic ketogenesis will promote hyperketonaemia and may facilitate development of pregnancy ketosis. It aggravates hypoglycaemia by inhibiting hepatic glucose production, and increases negative energy

balance by inhibiting uptake and utilisation of glucose by peripheral tissues (Schlumbohm & Harmeyer, 2004). These effects on glucose metabolism occur, whilst sensitivity of the peripheral tissues to insulin is decreased and the demand for glucose by the foeto-placental unit, is markedly increased (Rumball *et al.*, 2008). The energy needs of peripheral tissues and the foeto-placental unit may no longer be met, thus leading to an increased rate of lipolysis and a further increase in the rate of hepatic ketone body production (De Koster & Opsomer, 2013).

Chalmeh *et al.* (2015) revealed that NEFA levels were higher in early and mid lactation and close-up dry cows before glucose infusion and for all different hours following glucose infusion. These results indicated activation of lipid mobilisation – another metabolic mechanism of adaptation to these periods. In fact, it is well known that low insulin concentration and reduced insulin sensitivity of the tissues around parturition increase lipid mobilisation and induce further rises in plasma NEFA concentrations (Hayirli, 2006). The early decrease of NEFA values after the glucose administration demonstrates that lipid mobilisation of fatty acids is reduced in positive energetic balance condition. According to Grummer *et al.* (2004), the increase of plasma NEFA concentration led to the increase of ketogenesis by hepatocytes.

In the present study, BHBA and NEFA levels at 4 weeks before parturition were significantly higher than other periods (Table 1). After dextrose administration, the circulating BHBA profile followed the same pattern of NEFA concentration (Table 1). The early decrease of BHBA and NEFA in response to glucose administration was seen in all studied pe-

riods and it may demonstrate that following glucose infusion, the production of ketone bodies was reduced.

Nazifi *et al.* (2002) stated that pregnancy had a significant effect on serum lipids and cholesterol concentrations in lipoproteins of Iranian fat-tailed sheep, as with progression in the pregnancy period there was an increase in cholesterol and TG concentrations. Higher levels of lipid profile parameters were however detected at post parturition periods in Ghezel ewes (Table 2). These variations appear to reflect increased hepatic TG synthesis and VLDL secretion, because of the activities of lipoprotein lipase and hepatic lipase: the enzymes responsible for the catabolism of VLDL and their remnants (Nazifi *et al.*, 2005).

Serum concentrations of lipid profile were not changed after bolus intravenous glucose administration in all studied periods (Table 2). The slightly changing patterns of HDL and LDL following hypertonic dextrose administration may be due to the controlling role of glucose on the excretion of these lipoproteins from the liver to the bloodstream. There were no significant alterations of VLDL because the low capability of the liver of ruminants to excrete VLDL to the circulation (De Koster & Opsomer, 2013).

Numerous physiological, pathological and pharmacological stimuli influence thyroid hormone metabolism (Mooradian *et al.*, 2006). The results of the present study showed that serum levels of thyroid hormones changed following glucose infusion (Table 3). During intravenous dextrose administration, T3 was decreased in pregnant ewes and increased in non-pregnant, lactating ones. It may be suggested that glucose has a key role in regulation of T3 secretion in bloodstream (Table 4). The decreasing patterns of T3 at

pre-parturition periods may be due to high metabolic demands at these times. However, the slight changes of T4 following dextrose administration may be due to low or indirect effects of glucose on this hormone in Ghezel ewes.

Chalmeh *et al.* (2015) showed the significant and obvious changes of serum T3 and T4 after dextrose administration in the cows experiencing negative energy balance. It was suggested that providing the source of energy, as bolus intravenous glucose, could resolve the negative energy balance and change serum levels of thyroid hormones. Furthermore, Djoković *et al.* (2007) detected the hypothyroidal status in ketotic cows and the low circulating glucose concentration in them.

Cortisol fluctuates during pregnancy and parturition in dairy cows (Chalmeh *et al.*, 2015) and the results of the present study showed the alterations of this hormone at pre and post parturition periods in Ghezel ewes. Furthermore, the changing pattern of cortisol following intravenous dextrose administration could be useful for better understanding the regulation of energy related metabolism and the endocrine homeostasis to hyperglycaemic conditions in sheep. Previous studies revealed that the secretion of insulin in response to a small glucose load following intravenous glucose administration was diminished by cortisol treatment (Iqbal *et al.*, 2006) and the mechanism of this action remained obscure.

The concentration of IGF-1 can be seen as an indicator of the metabolic state of the dairy cow (Taylor *et al.*, 2004). Abribat *et al.* (1993) showed that the levels of IGF-1 were lower at the start of lactation and increased during the whole lactation, inversely related to milk yield. The results of the current study showed decreasing patterns of IGF-1 in all studied

periods (Table 3). Other researchers also mentioned acute decreases in circulating IGF-1 in response to increases in insulin or glucose (Lucy *et al.*, 2013). It may be suggested that glucose had obvious effect on metabolism of this hormone in Ghezel ewes. Dampney *et al.* (2013) showed that IGF-1 concentration was positively correlated with insulin ($r=0.377$; $P<0.001$) and glucose ($r=0.249$; $P<0.05$). This suggests that energy status or energy intake may regulate plasma concentrations of IGF-1. Ciccioli *et al.* (2003) also observed a positive correlation between plasma IGF-1, insulin and glucose concentrations in Angus $\times$ Hereford primiparous cows.

In the current research, the lowest prolactin levels were detected 2 weeks before parturition and increased after it (Table 3). Arai & Lee (1967) revealed that prolactin was low during months 3 and 4 of pregnancy in sheep, and then increased after parturition. Prolactin is a primary component of the galactopoietic complex of hormones. It may affect the lactogenesis in ruminants. Blood concentrations of prolactin in ruminants generally seem to be effective for maximal milk yield. Some evidence indicated that a 2-hour infusion of prolactin into lactating goats starting 30 minutes after milking may result in a slight (2.6%) but statistically significant increase in milk yield (Jacquemet & Prigge, 1991). Prolactin plays a part in partitioning nutrients between body tissue and milk (Hart, 1973). Apparently, the concentration of prolactin in the circulation can be reduced without markedly affecting milk secretion. The administration of exogenous prolactin during lactation has little or no effect on lactational performance of high yielding dairy cows (Wall *et al.*, 2006). The results of the present study showed that prolactin was significantly increased following in-

travenous dextrose administration 4 and 2 weeks before and 2 weeks after parturition (Table 3). However, its levels were decreased at remaining periods. It may be suggested that the production/excretion of prolactin in Ghezel ewes was energy dependent and glucose had a key role in determining the circulating prolactin concentrations (Table 4).

In conclusion, the present study revealed that the circulating metabolic profile of Ghezel ewes was strongly related to glucose (Table 4). It may be stated that bolus intravenous hypertonic dextrose administration could induce obvious endocrine and metabolic responses in this breed via providing a source of energy. Finally, the results of the current research showed that glucose may be an important direct controller of metabolic interactions in Ghezel ewes at different pre and post parturition periods.

REFERENCES

- Abell, L. L., B. B. Levy, B. B. Brodie & F. E. Kendall, 1952. A simplified method for the estimation of total cholesterol in serum and determination of its specificity. *Journal of Biological Chemistry*, **195**, 357–366.
- Abribat, T., P. Brazeau, I. Davignon & D. R. Garrel, 1993. Insulin-like growth factor-I blood levels in severely burned patients: Effects of time post injury, age of patient and severity of burn. *Clinical Endocrinology*, **39**, 583–589.
- Arai, Y. & T. H. Lee, 1967. A double-antibody radioimmunoassay procedure for ovine pituitary prolactin. *Endocrinology*, **81**, 1041–1046.
- Balikci, E., A. Yildiz & F. Gurdogan, 2007. Blood metabolite concentrations during pregnancy and postpartum in Akkaraman ewes. *Small Ruminant Research*, **67**, 247–251.

- Bell, A., W. S. Burhans & T. R. Overton, 2000. Protein nutrition in late pregnancy, maternal protein reserves and lactation performance in dairy cows. *Proceedings of the Nutrition Society*, **59**, 119–126.
- Burtis, C. A. & E. R. Ashwood, 1994. Tietz Textbook of Clinical Chemistry, 2^{ed} ed, W. B. Saunders Com, Philadelphia, pp. 735–888.
- Ciccioli, N., R. Wettemann, L. Spicer, C. Lents, F. White & D. Keisler, 2003. Influence of body condition at calving and postpartum nutrition on endocrine function and reproductive performance of primiparous beef cows. *Journal of Animal Science*, **81**, 3107–3120.
- Chalmeh, A., A. Hajimohammadi & S. Nazifi, 2015. Endocrine and metabolic responses of high producing Holstein dairy cows to glucose tolerance test based on the stage of lactation. *Livestock Science*, **181**, 179–186.
- Connolly, C. C., L. M. Aglione, M. S. Smith, D. B. Lacy & M. C. Moore, 2004. Pregnancy impairs the counter regulatory response to insulin induced hypoglycemia in the dog. *American Journal of Physiology - Endocrinology and Metabolism*, **287**, 480–488.
- Dampthey, J., F. Obese, G. Aboagye & R. Ayizanga, 2013. Correlations among concentrations of some metabolic hormones and nutritionally-related metabolites in beef cows. *Online Journal of Animal and Feed Research*, **3**, 176–180.
- De Koster J. D. & G. Opsomer, 2013. Insulin resistance in dairy cows. *Veterinary Clinics: Food Animal Practice*, **29**, 299–322.
- Djoković, R., H. Šamanc, M. Jovanović & Z. Nikolić, 2007. Blood concentrations of thyroid hormones and lipids and content of lipids in the liver of dairy cows in transitional period. *Acta Veterinaria Brno*, **76**, 525–532.
- Firat, A. & A. Ozpinar, 1996. The study of changes in some blood parameters (glucose, urea, bilirubin, AST) during and after pregnancy in association with nutritional conditions and litter size in ewes. *Turkish Journal of Veterinary and Animal Sciences*, **20**, 387–393.
- Friedewald, W. T., R. I. Levy & D. S. Fredrickson, 1972. Estimation of the concentration of low density lipoprotein cholesterol without the use of the preparative ultracentrifuge. *Clinical Chemistry*, **18**, 499–502.
- Grummer, R. R., D. G. Mashek & A. Hayirli, 2004. Dry matter intake and energy balance in the transition period. *Veterinary Clinics: Food Animal Practice*, **20**, 447–470.
- Harmeyer, J. & C. Schlumbohm, 2006. Pregnancy impairs ketone body disposal in late gestating ewes: Implications for onset of pregnancy toxemia. *Research in Veterinary Science*, **81**, 254–264.
- Hart, I. C., 1973. Effect of 2-bromo-ergocryptine on milk yield and the level of prolactin and growth hormone in the blood of the goat. *Journal of Endocrinology*, **57**, 179–180.
- Hawagane, S. D., S. B. Shinde & D. N. Rajguru, 2009. Haematological and blood biochemical profile in lactating buffaloes in and around Parbhani city. *Veterinary World*, **2**, 467–469.
- Hayirli, A., 2006. The role of exogenous insulin in the complex of hepatic lipidosis and ketosis associated with insulin resistance phenomenon in postpartum dairy cattle. *Veterinary Research Communications*, **30**, 749–774.
- Herdt, T. H., 2000. Variability characteristics and test selection in herd-level nutritional metabolic profile testing. *Veterinary Clinics: Food Animal Practice*, **16**, 387–403.
- Iqbal, J., Y. Kurose, B. Canny & I. J. Clarke, 2006. Effects of central infusion of ghrelin on food intake and plasma levels of growth hormone, luteinizing hormone, prolactin, and cortisol secretion in sheep. *Endocrinology*, **147**, 510–519.
- Jacquemet, N. & E. C. Prigge, 1991. Effect of increased post milking prolactin concentrations on lactation, plasma metabolites,

- and pancreatic hormones in lactation goats. *Journal of Dairy Science*, **74**, 109–114.
- Kaneko, J. J., J. W. Harvey & M. L. Bruss, 2008. *Clinical Biochemistry of Domestic Animals*. 5th ed, No. VIII. Academic Press.
- Lucy, M., R. Escalante, D. Keisler, W. Lamberson & D. Mathew, 2013. Short communication: Glucose infusion into early postpartum cows defines an upper physiological set point for blood glucose and causes rapid and reversible changes in blood hormones and metabolites. *Journal of Dairy Science*, **96**, 5762–5768.
- Mavrogiani, V. S. & C. Brozos, 2008. Reflections on the causes and the diagnosis of peri-parturient losses of ewes. *Small Ruminant Research*, **76**, 77–82.
- McGowan, M. W., J. D. Artiss, D. R. Strandbergh & B. Zak, 1983. A peroxidase coupled method for the colorimetric determination of serum triglycerides. *Clinical Chemistry*, **29**, 538–542.
- Mooradian, A. D., Haas, M. J. & Wong, N. C. W. 2006. The effect of select nutrients on serum high-density lipoprotein cholesterol and apolipoprotein A-I levels. *Endocrine Reviews*, **27**, 2–16.
- Morgante, M., 2004. Digestive disturbances and metabolic-nutritional disorders. In: *Dairy Sheep Nutrition*, eds. G. Pulina, R. Benici, International Publishing CAB, Wallingford, UK, pp. 165–190.
- Nazifi, S., M. Saeb & S. M. Ghavami, 2002. Serum lipid profile in Iranian fat-tailed sheep in late pregnancy, at parturition and during the post-parturition period. *Journal of Veterinary Medicine. A, Physiology, Pathology, Clinical Medicine*, **49**, 9–12.
- Nazifi, S., M. Saeb, S. Rategh & A. Khojandi, 2005. Serum lipids and lipoproteins in clinically healthy Caspian miniature horses. *Veterinarski Arhiv*, **75**, 175–182.
- Rumball, C. W. H., J. E. Harding, M. H. Oliver & H. Bloomfield, 2008. Effects of twin pregnancy and periconceptional undernutrition on maternal metabolism, fetal growth and glucose–insulin axis function in ovine pregnancy. *The Journal of Physiology*, **586**, 1399–1411.
- Schlumbohm, C. & J. Harmeyer, 2004. Hyperketonemia impairs glucose metabolism in pregnant and non-pregnant ewes. *Journal of Dairy Science*, **87**, 350–358.
- Taylor, V., Z. Cheng, P. Pushpakumara, D. Wathes & D. Beever, 2004. Relationships between the plasma concentrations of insulin-like growth factor-I in dairy cows and their fertility and milk yield. *The Veterinary Record*, **155**, 583–588.
- Van Saun, R. J., 2000. Pregnancy toxemia in a flock of sheep. *Journal of the American Veterinary Medical Association*, **217**, 1536–1539.
- Wall, E. H., H. M. Crawford, S. E. Ellis, G. E. Dahl & T. B. McFadden, 2006. Mammary response to exogenous prolactin or frequent milking during early lactation in dairy cows. *Journal of Dairy Science*, **89**, 4640–4648.
- Wathes, D. C., Z. Cheng, W. Chowdhury, M. A. Fenwick, R. G. Fitzpatrick, D. Morris, J. Patton & J. J. Murphy, 2009. Negative energy balance alters global gene expression and immune responses in the uterus of postpartum dairy cows. *Physiological Genomics*, **39**, 1–13.

Paper received 27.02.2018; accepted for publication 10.05.2018

Correspondence:

Aliasghar Chalmeh,
Department of Clinical Sciences,
School of Veterinary Medicine,
Shiraz University, Shiraz, Iran,
P.O. Box: 71345; tel: +98 711 6138700;
fax: +98 711 2286940,
e-mail address: achalmeh81@gmail.com