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PREGNANCY-RELATED CHANGES OF THE BLOOD BIOCHEMICAL PROFILE IN OULED DJELLAL EWE'S BREED UNDER SEMI-ARID CONDITIONS (ALGERIA)

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ABSTRACT

In mammals, the pregnant female carries many physiological and anatomical changes. Biochemical profiles are very important tools for monitoring gestation progress. This study was designed to investigate pregnancy-related changes of blood metabolites in Ouled Djellal ewes under semi-arid conditions. Blood samples were collected from ten non pregnant multiparous ewes 4 weeks before conception and 4, 12 and 18 weeks of pregnancy age. The pattern of changes of some biochemical parameters were studied. Cholesterol level showed no significant changes during pregnancy, while triglyceride, AST and Ca decreased up to the 12th week of pregnancy, whereas the total protein, albumin, and creatinine increased toward the 12th week of pregnancy. Urea reached maximum levels at the end of the pregnancy, contrary to ALT that was significantly decreased. Glucose concentration showed a continual decrease varying from 2.08 ± 0.78 g.l^{-1} at the first month of pregnancy to 0.35 ± 0.36 g.l^{-1} at the 18th week of pregnancy. On the other hand, pregnancy establishment increased significantly the glucose, triglyceride, albumin, and urea, but it decreased significantly the cholesterol and creatinine levels. No differences were observed between pregnant and non-pregnant ewe for the rest of the parameters. These results demonstrated a clear evidence of pregnancy-related distribution of blood biochemical indices of Ouled Djellal ewe under semi-arid conditions. Some substrates and enzymes were mainly higher during the first half of pregnancy (triglyceride, AST and Ca), and some others increased from the mild pregnancy period (total protein, albumin and creatinine), while urea and ALT changes were observed at late pregnancy. The energetic demand increased with advancing pregnancy.

Key words: blood biochemical parameters; ewe; pregnancy; prior to mating; semi-arid area

INTRODUCTION

In North Africa, sheep raising is concentrated in the steppe. The Ouled Djellal (OD) breed is the most dominant in Algeria representing nearly 63 % of the 28.4 million heads [34]. In the arid and semi-arid zones where the dry periods are long and the rainfall is low, the food intake is generally deficient in digestible energy and in proteins [13].

The biochemical monitoring during the different production phases could provide some advantages to producers in relation to changes in normal and abnormal metabolism leading to some metabolic disorders [31]. It is considered as an important procedure for complementary diagnosis by determining the various indicators in the blood of animals [54], particularly in pregnant females [36].

Important endocrine changes during the pregnancy period lead to increase nutrient flow to the pregnant uterus for high synthetic activities and energy yielding processes. Concomitantly; breed, age, malnutrition, foetal growth and season affected the blood serum chemistry values [29]. Glucose as a source of energy is the major metabolite used by the sheep foetus, who utilizes about one-third to one-half of the daily glucose turnover of 100 g [30]. The nutrient requirements of ewes increase during late pregnancy due to the rapid growth of the foetus (eighty percent of foetal growth occurs in the last 2 months). These needs are even higher according to the number of foetuses (180 g.day^{-1} ewes with two foetuses against 90 g in empty ewes). At this stage, the ewe needs to cover at least half of its energy requirement to avoid neoglycogenesis [20]. It is estimated that neosynthesized glucose accounts for 60 to 90 % of requirements [35]. In the event of a failure to cover energy needs, body fat is the first resource to be mobilized. Serum lipid and lipoprotein profiles are helpful when interpreted in conjunction to predict periparturient problems and for the diagnosis of metabolic diseases and the assessment of the nutritional status of animals [44]. The evaluation of urea level and liver enzymes (for example; glutamate dehydrogenase GLDH and aspartate aminotransferase AST) are strongly recommended in pregnant females as an indicators of efficiency of protein nutrition and of metabolism level, respectively [45]. The blood calcium (Ca) profile important is an important ionogram test to explore skeleton components, activity of enzyme systems, including those necessary for the transmission of nerve impulses and for the contractile properties of muscles and blood coagulation [26].

The objective of this study is to investigate pregnancy-related changes of blood biochemical parameters as indicators of the metabolic needs at different stages of pregnancy in Ouled Djellal ewes under semi-arid area.

MATERIALS AND METHODS

Animals and treatments

This trial was carried out in Ksar Sbahi region, Department of Oum El Bouaghi, Algeria (north-east Algeria with a Mediterranean climate type continental semi-arid, latitude 36° 5'N, longitude 7° 15'W and altitude 850 m). The experiment was performed during the breeding season (September) for ewes on ten adult non-lactating, non-pregnant, multiparous (3.6 ± 0.51 years) and clinically healthy Ouled Djellal ewes. They averaged 57.22 ± 6.99 kg mean body weight and were raised in a semi-intensive system under natural lighting. They were allowed to drink and to feed freely, the ration consisted of hay supplemented by pelleted concentrate of 14 % protein and barley as a source of energy throughout the experiment period.

To ensure synchronized mating, oestrus was induced using intravaginal sponges that contained 40 mg fluorogestone acetate (Synchropart), which was inserted for 14 days and intramuscular injection of 500 IU of eCG (Folligon) 24 h before sponge withdrawal. After removing sponges, the fertile rams were introduced for natural mating. All ewes became pregnant at first mating.

Collection of samples

The first blood samples were withdrawn once from all ewes, 4 weeks before mating. The second sampling step coincides with the 4th, 12th and 18th week of pregnancy. Jugular blood samples (4 ml) were collected in a heparinized tube early in the morning before feeding. The time interval between collection and transportation to the laboratory generally took less than 60 min. The collected blood samples were promptly transported to the laboratory, and centrifuged for 10 min at 3000 × g. Plasma glucose, total protein, albumin, urea, creatinine, triglycerides, cholesterol, ALT-alanine aminotransferase, AST-aspartate aminotransferase, and Ca-calcium were determined with the use of commercial kits (SEAC, Florence, Italy) and measured using the UV Spectrophotometer (SEAC, Slim, Florence, Italy).

Statistical analysis

Mean values were computed for various parameters. Repeated measures test followed by Bonferroni *post hoc* test was performed to compare pregnancy-related means at different study stages. The T-test was used to compare averages of plasma metabolites 4 weeks before mating and pregnancy period. A partial correlation test was run to determine the relationship between biochemical parameters whilst controlling for pregnancy and before mating. For each test, a P-value of less than 0.05 was considered statistically significant. These tests were done with the aid of SPSS version 24.

Ethical statement

All procedures performed in this study involving experimental animals complied with the Algerian Ethics Legislation (Ordinance No. 06-05 of 15 July 2006) and were approved by the Batna 2 University, Batna, Algeria.

RESULTS

Pregnancy had a significant effect on the plasma glucose concentrations of Ouled Djellal ewe, as with progression in the pregnancy period there was a decrease towards the 18th week (Table 1). The comparison between 4 weeks before mating and the pregnancy period showed also a significant variation (P < 0.01) with the increase of glucose needs during pregnancy (Fig. 1). In addition, plasma glucose had a significant positive correlation with triglyceride (r = + 0.62), urea (r = + 0.43), AST (r = + 0.41), ALT (r = + 0.58) and Ca (r = + 0.39). However, there was a negative correlation with the rest of the parameters (Table 2).

Table 1. Mean (± S.E.M.) plasma metabolite concentrations at 4, 12 and 18 weeks in pregnant Ouled Djellal ewe (n = 10).

Parameters	Pregnancy (weeks)		
	4	12	18
Glucose ($g.l^{-1}$)	2.08 ± 0.78^a	0.52 ± 0.06^b	0.35 ± 0.16^c
Triglyceride ($g.l^{-1}$)	0.50 ± 0.26^a	0.12 ± 0.05^b	0.19 ± 0.02^b
Cholesterol ($g.l^{-1}$)	0.67 ± 0.09^a	0.62 ± 0.06^a	0.65 ± 0.07^a
Total protein ($g.l^{-1}$)	60.32 ± 4.44^a	72.76 ± 4.38^b	67.78 ± 3.60^b
Albumin ($g.l^{-1}$)	24.95 ± 0.83^a	27.54 ± 1.02^b	26.70 ± 0.38^b
Urea ($g.l^{-1}$)	0.24 ± 0.06^a	0.24 ± 0.04^a	0.38 ± 0.04^b
Creatinine ($mg.l^{-1}$)	7.13 ± 0.58^a	13.60 ± 0.76^b	12.35 ± 1.10^b
AST (IU)	122.12 ± 22.86^a	102.57 ± 13.21^b	108.04 ± 11.18^b
ALT (IU)	30.85 ± 8.45^a	$22.00 \pm 6.98^{a,b}$	20.20 ± 6.57^b
Calcium ($mg.dl^{-1}$)	111.10 ± 7.46^a	92.30 ± 10.05^b	99.90 ± 6.70^b

a, b, c – The same letters indicate that no significant differences (P > 0.05) were detected between the groups

Statistical analysis showed that triglyceride concentrations were higher in pregnant compared to non-pregnant Ouled Djellal ewe. Their levels showed a significant decrease towards the 12th week of pregnancy (0.50 ± 0.26 vs. 0.12 ± 0.05) followed by a non-significant increase during the end of pregnancy (0.12 ± 0.05 vs. 0.19 ± 0.12).

Cholesterol plasma levels showed no significant change (P > 0.05) as pregnancy proceeds (Table 1). However, this substrate concentration showed significantly high level in non-pregnant compared to pregnant ewes (0.79 ± 0.14 vs. 0.65 ± 0.05 $g.l^{-1}$; P < 0.05). There was no correlation between cholesterol and other biochemical parameters (Table 2).

This present study showed that plasma total protein increased significantly (60.32 ± 4.44 vs. 72.76 ± 4.38) towards the 12th week of pregnancy and then remained high without significant change during the end of pregnancy (72.76 ± 4.38 vs. 67.78 ± 3.60; P > 0.05). There was a non-significant difference in blood total protein between

Table 2. Partial correlation between different parameters

	Glu	TG	Chol	TP	Alb	Urea	Creat	AST	ALT	Ca
Glu	1									
TG	0.62***	1								
Chol	-0.13	0.01	1							
TP	-0.45**	-0.47**	0.09	1						
Alb	-0.39*	-0.26	0.09	0.49**	1					
Urea	0.43**	0.50**	-0.04	-0.39*	-0.34*	1				
Creat	-0.79***	-0.66***	0.15	0.61***	0.53**	-0.43**	1			
AST	0.41**	0.16	-0.17	-0.39*	-0.33*	0.11	-0.32*	1		
ALT	0.58***	0.25	-0.07	-0.20	-0.24	0.12	-0.41**	0.60***	1	
Ca	0.39*	0.27	-0.21	-0.31	-0.23	0.04	-0.46**	0.30	0.43**	1

Glu – Glucose; TG – Triglyceride; Chol – Cholesterol; TP – Total protein; Alb – Albumin; Creat – Creatinine; AST – Aspartate aminotransferase; ALT – Alanine aminotransferase; Ca – Calcium; *P < 0.05; ** P < 0.01; ***P < 0.001.

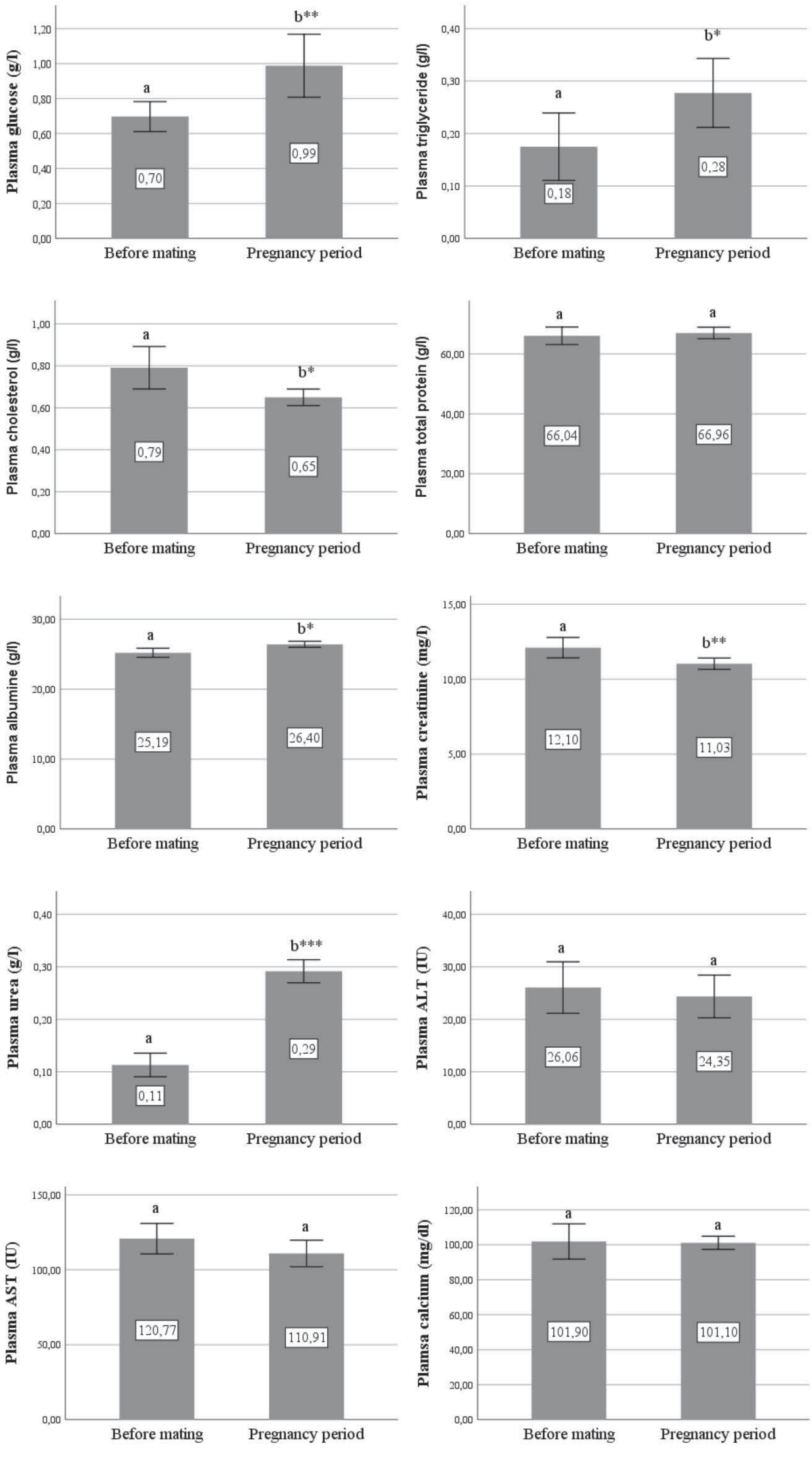

Fig. 1. Mean (± CI) plasma metabolite concentrations 4 weeks before mating and pregnancy period in ewes (n = 10).
CI – confidence interval; Pregnancy period – average pregnancy weeks; a, b – the same letters indicate no statistically significant differences between the groups (P > 0.05); *P < 0.05 ; ** P < 0.01; ***P < 0.001.

pregnant and non-pregnant ewes (Fig. 1). Plasma albumin and creatinine levels increased significantly at 12th week of pregnancy (27.54 ± 1.02 $g.l^{-1}$ and 13.60 ± 0.76 $mg.l^{-1}$; respectively) followed by a non-significant decrease during the end of pregnancy (26.70 ± 0.38$g.l^{-1}$ and 12.35 ± 1.10$mg.l^{-1}$, respectively). Pregnant ewes had significantly higher albumin concentration (P < 0.05) while non-pregnant ewes had higher creatinine levels (P < 0.01). There were significant negative correlations between creatinine and glucose, triglyceride, urea respectively (r = -0.79; r = -0.66 and r = -0.43).

Plasma urea began to increase from the 12th week of pregnancy (Table 1). Our results showed that a low level of urea is reported 4 weeks before mating compared to the pregnancy period (P < 0.001) (Fig. 1).

The enzymes pattern of change showed a significant decrease in AST level towards the 12th week of pregnancy (102.57 ± 13.21 IU). However, ALT concentration was higher in early pregnancy than in late pregnancy (30.85 ± 8.45 vs. 20.20 ± 6.57 IU; P < 0.05). Otherwise, there were no significant changes (P > 0.05) in transaminases between 4 weeks before mating and the pregnancy period (Fig. 1). Transaminases were positively correlated with glucose and negatively correlated with protein, albumin, and creatinine (Table 2). Calcium level showed a significant decrease toward the 12th week of pregnancy.

DISCUSSION

This study has been conducted to investigate the physiological changes on blood constituents of pregnant Ouled Djallel ewes, kept under semi-arid conditions in north-eastern Algeria. The obtained results would be useful to understand pregnancy requirements based on blood biochemical profile and to implement strategic management using sheep reproduction synchronization to avoid metabolic and health disorders.

Consistent with our findings, Chikhaoui et al. [10] and Ismaeel et al. [27] observed a significant decline in glucose concentration as pregnancy progressed. However, Charismiadou et al. [9] noted peak plasma glucose levels on the final day of pregnancy. The decreased glucose levels during late pregnancy are linked to foetal development and the transfer of maternal glucose to foetal circulation [16, 27], particularly in the later stages of gestation, when foetal liver and muscle glycogen content increases rapidly [22]. Late pregnancy poses significant metabolic challenges for ewes, particularly due to increased foetal size, which places additional stress on maternal carbohydrate metabolism [52]. Gluconeogenesis serves as the primary source of blood glucose in ruminants; therefore, reduced cortisol levels during late pregnancy may inhibit gluconeogenesis [41].

In this study our animals were pregnant during winter and then they were exposed to cold stress which reduces insulin secretion and, in consequently, glucose consumption. This disrupted energy balance may have led to alterations in circulating metabolic markers [2]. Furthermore, ewe responsiveness to insulin was significantly reduced during late pregnancy, which led to decrease glucose turnover and uptake by muscle and fat tissues [24, 51]. Pregnant Ouled Djellal ewes showed a significant increase in glucose needs compared to non-pregnant ewes. This result is analogous to Al-Dewachi [1] and it is in contradiction to Firat and Ozpinar [19]. Negative energy balance in pregnant ewes appears to be linked to the glucose requirements of the foetal-placental unit, primarily relying on glucose and lactate for energy [35]. Placental progesterone has a significant role in modulating insulin release during pregnancy [49], leading to increased glucose levels [50]. Adrenal corticoid concentration (ACHs) rises during pregnancy [25], mainly involved in mobilizing body protein amino acids (AA), resulting in hepatic deamination and the conversion of some α-ketoacids to glucose at an accelerated rate [22]. Mahmoud and Azab [41] suggest that glucose regulation during late pregnancy is predominantly influenced by cortisol.

Plasma triglyceride concentration in pregnant Ouled Djellal ewes registered significant decrease (P < 0.05) towards the 12th week of pregnancy. In late pregnancy, while the authors Gaadee and Gehan [21] and Lotfollahzadeh et al. [37] reported an increase in serum triglyceride levels, others noted fluctuations. Christie [11] observed a decline in plasma lipid content followed by a surge near parturition, while Nazifi et al. [44] found rising plasma triglyceride levels. Pregnancy stages exhibit distinct lipid metabolism patterns, with early reliance on dietary carbohydrates and increased lipolytic activity later. Triglyceride elevation in late pregnancy may relate to insulin, whose effectiveness decreases. Insulin resistance may develop alongside hormonal changes, predisposing ewes to increased cholesterol and triglyceride levels. Pregnant Ouled Djellal ewes showed elevated triglyceride levels, consistent with Al-Dewachi [1] and Hamadeh [23]. Reduced triglyceride levels in later pregnancy may signal increased insulin resistance [56].

The pregnancy period in the present study had no significant influence on plasma concentration of cholesterol. Our findings of the lack significant changes in cholesterol levels during pregnancy align with those reported by Chikhaoui et al. [10]. Conversely, Berkani et al. [5], Nazifi et al. [44], Ozpinar and Firat [46], and Ramos et al. [47] observed a notable increase towards the end of pregnancy. Mobilization of fatty acid reserves during energy deficiency at the end of pregnancy or lactation requires lipoproteins, primarily composed of cholesterol and its esters, for transport. Our results corroborate those of Ismaeel et al. [27], showing higher cholesterol concentrations in non-pregnant than pregnant ewes. However, our findings contradict those of Al-Dewachi [1] and Hamadeh [23], who observed higher cholesterol levels in pregnant ewes. Increased hormone levels associated with pregnancy may contribute to elevated cholesterol levels, stimulated by rising leptin concentrations [27, 31, 43, 55].

Plasma total protein levels significantly increased ($P < 0.05$) by mid-gestation and remained elevated ($P > 0.05$) until the end of gestation (Table 1). However, Brzostowski et al. [8] and El-Sherif and Assad [17] observed a decline in blood protein concentrations during later gestational stages. Manns and Lewing [42] suggest that the slight rise in total protein levels on the 14th day of pregnancy may result from embryo-specific protein production during maternal recognition of pregnancy. Maternal serum protein concentrations decrease due to accelerated foetal growth and increased amino acid utilization [28]. Despite glucose and lactate being crucial foetal fuels, amino acids play a key role in sheep foetal energy metabolism [18]. The decrease in serum total protein, primarily driven by a decline in globulin, especially alpha 1 and gamma fractions, may be attributed to globulin-rich colostrum production. Sheep demonstrate the ability to synthesize milk constituents 3 to 4 weeks prepartum [12]. Nevertheless, El-Sherif and Assad [17] observed a gradual increase in plasma proteins in pregnant ewes, peaking at parturition. In contrast to our findings, Lynch et al. [39] noted an increased protein requirement in gestating ewes.

Albumin is synthesized in the liver and is the protein primarily responsible for the oncotic pressure in plasma [33, 48]. Blood samples can also be analyzed for albumin which reflects longer-term protein status and liver function [40]. The albumin level represents the total protein's storage capacity when the diet contains low protein, in which case the urea is recycled via saliva to the rumen and little nitrogen is lost [38]. Serum albumin concentrations fall during the last month of gestation as immunoglobulins are manufactured and accumulate in the udder, thus serum albumin concentrations in the region of 26 to 30 $g.l^{-1}$ are "normal" during the last month of gestation [40].

Urea, formed from ammonia released during amino acid metabolism, serves as an indicator of protein utilization [7]. Our study, in line with El-Sherif and Assad [17], highlights an elevation in plasma urea levels throughout pregnancy, peaking around the 10th week and reaching maximum at parturition. However, conflicting observations exist; Brzostowski et al. [8] noted high urea levels early in pregnancy followed by a decline, while Firat and Ozpinar [19] reported lower urea levels in pregnant ewes compared to non-pregnant ones. Conversely, our results oppose El-Sherif and Assad [17], who observed increased creatinine levels during late pregnancy. This discrepancy may indicate heightened liver and kidney activity to meet increased metabolic demands during gestation [17]. Plasma urea, though, inadequately reflects kidney function in sheep [7].

Our results corroborate those of El-Sherif and Assad [17] indicating a significant increase of transaminases from 2nd week of pregnancy. The increase in transaminases might indicate impairment in some muscle and liver cells due to rapid gluconeogenesis associated with pregnancy. Both enzymes were found to be involved in gluconeogenesis [17, 26]. It is well known that stress can affect transaminases activity, so it follows that sudden or abrupt changes could upset an animal enough to cause changes in enzyme activity owing to increased stimulation by corticoids [53]. The increase in transaminases might indicate impairment in some muscle and liver cells due to rapid gluconeogenesis associated with pregnancy. Both enzymes were found to be involved in gluconeogenesis [17, 26]. It is well known that stress can affect transaminases activity, so it follows that sudden or abrupt changes could upset an animal enough to cause changes in enzyme activity owing to increased stimulation by corticoids [53].

AST was proved to increase under the effect of glucocorticoids which are released more during pregnancy [17]. Severe exercises were reported to result in an increase in ALT [14]. According to Tibbo et al. [53], any factor which affects metabolism will affect transaminases.

During pregnancy, calcium transfer to foetuses reach maximum at parturition [6] so it mildly decreases in late pregnancy [3, 15]. Azab and Abdel-Maksoud [4] noted a significant decline in plasma calcium during late pregnancy, possibly due to increased foetal demands [32]. Despite increased intestinal calcium absorption throughout pregnancy, it remains insufficient for late pregnancy and early lactation, leading to increased bone resorption [6].

CONCLUSIONS

This study revealed significant changes in plasma biochemical parameters of Ouled Djellal ewes' reared under semi-arid conditions during pregnancy period. Glucose decreased progressively, while triglyceride levels initially rose, and then declined by the 12th week. Total protein increased notably by the 12th week, with no difference between pregnant and non-pregnant ewes. Enzyme levels varied, with AST decreasing by the 12th week and ALT higher in early pregnancy. Calcium levels significantly decreased by the 12th week. These findings underscore the dynamic metabolic shifts occurring during ovine gestation.

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have influence the work reported in this paper.

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