Elevated levels of blood urea nitrogen and creatinine in the last trimester of pregnancy of dromedary camels (*Camelus dromedarius*)

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Abstract:

**BACKGROUND:** The knowledge of blood parameters is important for assessing the physiological status and health of animals. **OBJECTIVES:** This study was conducted to determine the effect of heavy pregnancy on some serum indices of dromedary camels. **METHODS:** Twenty clinically healthy female dromedary camels aged between 4-5 years were divided into two equal groups: I: pregnant camels in their last trimester; and II: non-pregnant age-matched controls. The concentration of glucose, calcium, phosphorus, albumin, total protein, uric acid, blood urea nitrogen (BUN), creatinine and the activity of aspartate amino transferase (AST), alanine amino transferase (ALT), and gamma glutamyl transferase (GGT), was measured. **RESULTS:** The results of this study show that the concentrations of glucose, calcium and phosphorus remained unchanged in pregnant camels compared to non-pregnant ones. The concentrations of serum BUN and creatinine in pregnant camels were higher, and these aforementioned differences were significant (p=0.02 and 0.003 respectively). GGT activity was lower in pregnant than in non-pregnant camels (p=0.04). **CONCLUSIONS:** The increase in BUN and creatinine levels might be part of the homeorhetic mechanisms for adaptation of camels during heavy pregnancy. The high urea-recycling rate in camels may transfer urea to the gastrointestinal tract as a source of "non-protein nitrogen" instead of being excreted as urine. The reduction of GGT as at the time of heavy pregnancy, may be attributed to its conversion to glutathione, as an antioxidant.

Introduction

Camel (*Camelus dromedarius*) is a unique animal, in adapting to the harsh climatic conditions of the desert. Camels can tolerate prolonged water deprivation, high heat load, and poor quality feeds. The crucial role of the camel in the economic and social life of pastoralists in arid and semi-arid regions of several places in the world has been noted by researchers (Ouajd and Kamel, 2009; Gaughan, 2011). There is a wide range of mechanisms for coping against nutritional deficiencies in animals. Camels have more efficient fermentation in pre-stomach, high intestinal absorption of nutrients, high neoglucogenesis, low ketogenesis and a high lipomobilization, along with great urea recycling for proteins (Ouajd...
and Kamel, 2009). Pregnancy is a dynamic process characterized by dramatic physiological changes. The increase in metabolic functions during pregnancy results in alteration of the biochemical profile. The alteration in routine serum clinical biochemistry is yet to be properly studied, during the different stages of pregnancy in camels (Omidi et al., 2014). The liver metabolizes carbohydrates and lipids and also plays an essential role in amino acid metabolism (Ouajd and Kamel, 2009). To evaluate the health of the liver, some blood constituents and enzymes including aspartate amino transferase (AST), alanine amino transferase (ALT), and gamma-glutamyl transferase (GGT) were measured routinely. When the liver is injured, the enzymes within the hepatocytes enter the bloodstream (Woreta and Alqahtani, 2014). Total protein and albumin are the proteins made by the liver. Creatinine and blood urea nitrogen (BUN) are waste products removed from the blood by the kidneys. Creatinine is a breakdown product of creatine phosphate in the muscle. Serum creatinine is a marker used for renal function assessment (Kamili et al., 2013; Patel et al., 2013). High BUN usually means that kidney function is less than normal, but other factors may affect the BUN level. The aim of this study was to investigate the effect of heavy pregnancy on the indices of the liver and kidney health in the serum of dromedary camels.

Materials and Methods

This study was conducted on female Iranian single-humped camels in February 2013. The camels were reared at the camel breeding station (52 km away from the city of Zabol, 31°1’47” North latitude, 61°29’52” east longitude, and 478 m above the sea level) in Sistan and Baluchestan Province, Southeastern Iran. Twenty female camels, aged between four and five years were used for this study. The pregnant camels were selected in consultation with a cameleer who is conversant with their mating history. Ten non-pregnant and ten camels in their last three months of pregnancy were selected for this study. Blood samples (10 ml) were obtained from the jugular vein of camels and placed in vacuum containers at 6 p.m. for two consecutive days. The serum was prepared by removing the clot from the whole blood sample and subsequently centrifuged at 750 × g for 15 min. The sera were stored at −21°C awaiting analysis. The samples with hemolysis were discarded. The biochemical parameters were measured using a standard autoanalyser (Hitachi 717, Boehringer. Mannheim, Germany) by commercial kits (Parsazmoon, Co, Iran). The levels of total protein and albumin were determined by biuret reaction (Meyer et al., 1992) and bromocresol green dye binding method (Ueno et al., 2013), respectively. The activity of GGT was measured using the SZASZ method (Szasz, 1976), and those of AST and ALT were measured using the colorimetric method of Reitman and Frankel (1957). Serum enzyme activities were measured according to the specific reaction of each enzyme using basic standard techniques. Thereafter, the glucose level was determined after enzymatic oxidation in the presence of glucose oxidase as described by Barham and Trinder (1972). All data were expressed as SI units. In order to compare the two groups (pregnant and non-pregnant), the non-parametric Mann-Whitney U test was performed. The correlation between two parameters was analyzed using Spearman’s correlation test. All statistical calculations were performed using SPSS version 20 software. The experiment was approved by the animal welfare committee of the Agriculture Faculty of Birjand University.

Results

The concentrations of glucose, calcium, phosphorus, albumin, total protein, BUN, creatinine and uric acid, as well as the enzyme...
activity of AST, ALT and GGT in the blood serum of pregnant and non-pregnant camels are shown in Table 1. Physiological status and pregnancy period had a significant effect on the levels of BUN and creatinine. Lower serum levels of GGT were observed in pregnant camels. The Spearman rank correlation coefficients are shown in Table 2 for only those health indicators that significantly correlated with the concentration of at least one constituent. Eventually, all pregnant camels carried pregnancy to term and each delivered a calf.

## Discussion

In late pregnancy, the nutrient requirements increases to meet the growth requirements of the fetus. In the present study, glucose concentration remained without difference in pregnant camels. Thus, this finding is in line with that of Zvorc et al. (2006) in sows during pregnancy. Contrary to these findings, some researchers reported lower serum glucose levels in pregnant camels (Saeed et al., 2009), pregnant goats (Khan and Ludri, 2002), and pregnant sheep (Moallem et al., 2012). A wide variation in the blood glucose concentration of camels was reported. The glucose level of the blood ranged from 1.5 mmol/l in adult camels to 12 mmol/l in 7 day old calves (Yadav and Bissa, 1998). This wide range of glucose level may be attributed to the difference in age, sex, physiological conditions and seasonal differ-

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### Table 1. Serum levels of some variables in pregnant and non-pregnant camels (n=20). (1) Blood urea nitrogen, (2) Aspartate aminotransferase, (3) Alanine aminotransferase, (4) Glutamyl transferase. (*) significant at the 0.05 level. (**) significant at the 0.01 level.

<table>
<thead>
<tr>
<th>variable</th>
<th>Pregnant (n=10)</th>
<th>Non-pregnant (n=10)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25&lt;sup&gt;b&lt;/sup&gt;</td>
<td>50&lt;sup&gt;b&lt;/sup&gt; (medium)</td>
<td>75&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Glucose (mmol/l)</td>
<td>3.39</td>
<td>3.85</td>
<td>4.52</td>
</tr>
<tr>
<td>Calcium (mmol/l)</td>
<td>2.12</td>
<td>2.23</td>
<td>2.25</td>
</tr>
<tr>
<td>Phosphorus (mmol/l)</td>
<td>1.42</td>
<td>1.58</td>
<td>1.61</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>30.02</td>
<td>30.35</td>
<td>30.80</td>
</tr>
<tr>
<td>Total protein (g/l)</td>
<td>50.95</td>
<td>60.70</td>
<td>70.70</td>
</tr>
<tr>
<td>Uric acid (µmol/L)</td>
<td>0.47</td>
<td>0.50</td>
<td>0.50</td>
</tr>
<tr>
<td>BUN&lt;sup&gt;1&lt;/sup&gt; (mmol/l)</td>
<td>4.28</td>
<td>5.17</td>
<td>6.60</td>
</tr>
<tr>
<td>Creatinine (µmol/l)</td>
<td>80.44</td>
<td>89.28</td>
<td>97.24</td>
</tr>
<tr>
<td>AST&lt;sup&gt;2&lt;/sup&gt; (IU/l)</td>
<td>39.50</td>
<td>45.00</td>
<td>50.00</td>
</tr>
<tr>
<td>ALT&lt;sup&gt;3&lt;/sup&gt; (IU /l)</td>
<td>2.00</td>
<td>5.00</td>
<td>6.00</td>
</tr>
<tr>
<td>GGT&lt;sup&gt;4&lt;/sup&gt; (IU /l)</td>
<td>5.10</td>
<td>5.85</td>
<td>6.32</td>
</tr>
</tbody>
</table>

### Table 2. Correlation coefficients between the variables measured in pregnant and non-pregnant camels. (1) Alanine aminotransferase, (2) Aspartate aminotransferase, (3) Blood urea nitrogen, NS: Non-significant- (*) Correlation is significant at the 0.05 level (two-tailed)- (**) Correlation is significant at the 0.01 level (two-tailed).

<table>
<thead>
<tr>
<th>Variable A</th>
<th>Variable B</th>
<th>Pregnant camel (n=10)</th>
<th>Non-pregnant camel (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Glucose</td>
<td>0.77**</td>
<td>NS</td>
</tr>
<tr>
<td>ALT</td>
<td>Albumin</td>
<td>0.78**</td>
<td>NS</td>
</tr>
<tr>
<td>AST&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Albumin</td>
<td>0.68*</td>
<td>NS</td>
</tr>
<tr>
<td>AST</td>
<td>BUN&lt;sup&gt;3&lt;/sup&gt;</td>
<td>NS</td>
<td>0.66*</td>
</tr>
<tr>
<td>Albumin</td>
<td>Total protein</td>
<td>NS</td>
<td>0.79**</td>
</tr>
<tr>
<td>Albumin</td>
<td>Creatinine</td>
<td>NS</td>
<td>0.71*</td>
</tr>
<tr>
<td>Creatinine</td>
<td>Total protein</td>
<td>NS</td>
<td>0.81**</td>
</tr>
<tr>
<td>Creatinine</td>
<td>BUN</td>
<td>NS</td>
<td>0.72*</td>
</tr>
<tr>
<td>Total protein</td>
<td>BUN</td>
<td>NS</td>
<td>0.63*</td>
</tr>
</tbody>
</table>
ences (Barakat and Abdel-Fattah, 1971; Nazi- 
fi et al., 1999; Amin et al., 2007). The camels 
considered for the present study were of the 
same age and there was no seasonal variation in 
sampling time. Approximately, the low serum 
glucose concentration of camels in this study 
(3.85 mmol/l) may be attributed to protein 
and energy deficiency in the diet during win-
ter (Nazifi et al., 1999). Therefore, unchanged 
blood glucose concentrations in pregnant cam-
els need to be considered as a result of suffi-
cient homeostasis, in maintaining the concen-
tration of blood glucose in a constant range. In 
this study, calcium and phosphorus concentra-
tion remained unchanged in pregnant camels. 
Contrary to the results of this study, in vari-
ous investigations on pregnant camels (Saeed 
et al., 2009), Holstein cows (Nazifi and Sami, 
1997), and mares (Filipović et al., 2010), calci-
um and phosphorus levels were reported to be 
lower than that of the non-pregnant animals. The 
similar levels of calcium and phosphorus in 
pregnant and non-pregnant camels might be 
due to a balance between the increase in ab-
sorption of these minerals from the intestine 
and their sufficient supply to the fetus (Fudge 
and Kovacs, 2010). The range of total protein 
concentration reported by various researchers 
is 50.5 to 80.0 g/l in camels (Yadav and Bissa, 
1998). The higher serum levels of total protein 
and albumin observed in pregnant camels in 
comparison with nonpregnant camels were not 
significant (60.70 vs. 60.10 g/l and 30.35 vs. 
30.05 g/l respectively). The range of serum to-
tal protein in this study is in accordance with 
the study of Dowelmadina et al. (2012). During 
heavy pregnancy, there is abundant synthesis 
of proteins in the liver, and this is as a result of 
the higher energy requirement for fetal growth. 
Glucocorticoids improve the mobilization of 
extra hepatic proteins and transport amino ac-
ids to liver cells. The mobilized amino acids 
in liver cells are utilized during gluconeogen-
esis, which is the primal source of energy for 
the fetus (Satué and Montesinos, 2013). The 
slight increase in total protein concentrations 
in late pregnancy, is as a result of hormonal 
changes in the organism. The higher levels of 
total protein concentration in the blood plasma 
of pregnant mares compared to nonpregnant 
one were recorded by Milinković-Tur et al. 
(2005). The interpretation of variations in liv-
er and serum enzyme activities is complicated 
because the activity is affected by changes in 
the levels of cofactors, activators and inhibi-
tors, as well as by changes in the concentra-
tion of the enzyme itself. ALT and AST activities 
showed significant correlation with serum al-
bumin, corresponding to the higher activity 
of the liver along with natural mechanisms, 
which combat oxidative stress during heavy 
pregnancy. In the serum, albumin represents 
the major plasma antioxidant component (Lin 
et al., 2009). In pregnant camels, the positive 
correlations between ALT activity and glucose 
were seen. This finding revealed that the high-
er activity of the liver had a significant effect 
on glucose metabolism. Some researchers 
suggested that liver enzymes, especially ALT, 
were significantly associated with insulin re-
sistance in human diabetic patients (Zhang et 
et al., 2010). Insulin resistance in camels differs 
most likely with sheep and ponies. The high 
plasma glucose concentrations together with 
low insulin levels may be of advantage to 
camels with extremely poor quality feeds (El-
mahdiwt al., 1997). The correlations between 
some parameters in non-pregnant camels were 
positive. On the contrary, these correlations 
differed in pregnant camels, indicating homeo-
static mechanisms for each component. By 
comparing the obtained results, a statistically 
significant decrease in the GGT activity was 
recorded in the pregnant camels relating to the 
non-pregnant (5.85 vs. 6.70 IU/l). Similar find-
ing in pregnant mares have been found by Mil-
inković et al. (2005). They found that GGT ac-
tivity reached the lowest value in the final third 
of the pregnancy period. GGT is involved in 
the metabolism of glutathione (the most abun-
dant cellular thiol antioxidant), which plays an important role in maintaining the antioxidative status of the entire body (Chen et al., 2013). The most striking result of the present study is that, BUN and creatinine in pregnant camels were higher than non-pregnant ones and this difference was significant (p=0.02 and p=0.003, respectively). The quantity of creatinine formed each day depends on the total body content of creatine, which in turn depends on the dietary intake, rate of synthesis of creatine, and muscle mass (Patel et al., 2013). Camelids have very powerful mechanisms in urea recycling. Camels can recycle up to 90% of BUN, in contrast to ruminants, which present a value of 10 to 30%. The nitrogen recycling in camels increases in the case of lower proteins in diet and/or dehydration (Ouajd and Kamel, 2009). Camel has very particular anatomical structures in the kidney (Monjezi et al., 2014). Only a small volume of water is lost during the elimination of urea by the production of concentrated urine (Abere and Oguzor, 2011). Significantly higher BUN was recorded in pregnant camels (5.17 µmol/l) compared with the nonpregnant ones (3.92 µmol/l). The creatinine values observed in pregnant and non pregnant camels were similar to those previously published by other researchers (Kamili et al., 2013). Furthermore, the creatinine of pregnant camels (89.28 µmol/l) was significantly higher than nonpregnant camels (64.53 µmol/l). In the present study, the camels were not dehydrated or deprived of water but their access to feed supplies was limited. It is known that kidney function in camels is less sensitive to dehydration compared to other species (Kamili et al., 2013). Changes in the concentration of plasma creatinine depend not only on the renal excretion of creatinine, but also on its production and volume of distribution. The exceptionally high level of BUN in camels, in comparison to other livestock, is of interest in view of the camel’s ability to utilize urinary nitrogen at times of poor grazing or water deprivation. The highest value of BUN in the late pregnancy period was reported by Durak and Altinek (2006) in ewes. The high requirement for energy by pregnant ewes led to an increase in BUN level. In summary, the present study revealed that protein catabolism and high need for energy by pregnant camels, during the late trimester of the pregnancy period, may affect the catabolism of protein in the body resulting to an increase in BUN and creatinine levels. On the other hand, the high urea-recycling rate in camels may transfer urea to the gastrointestinal tract as a source of “non-protein nitrogen” instead of being excreted as urine. Kidney health indices must be cautiously interpreted especially in heavy pregnancy period. Further research should be done to investigate the physiologic state of the liver and kidney’s of dromedary camels experiencing a heavy pregnancy.

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سطح بالای ازت اوره خون و کراتینین در سه ماهه آخر آبستنی شتر تک کوهانه (Camelus dromedarius)

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چکیده
زمینه مطالعه: برای ارزیابی وضعیت فیزیولوژیک و سلامت حیوانات، دانش در مورد ترکیبات خونی نقش مهمی دارد. هدف این مطالعه با هدف تعیین اثر آبستنی سنگین بر برخی شاخص‌های سرمی شتر تک کوهانه انجام شد. روش کار: بست کردن گروهی از شترهای آبستنی در سه ماهه آخر آبستنی و یک گروه داده‌پذیر شده بودند. شترهای شاهد همسن در این مطالعه بهترین نتیجه‌رسانی‌ها داشتند.

روش کار:
مزایده نهایی:

نتایج: غلظت کلسیم و فسفر در شترهای آبستن نسبت به شترهای غیر آبستن افزایش یافت. افزایش غلظت BUN، فعالیت GGT، ALT و AST در شترهای آبستن نسبت به شترهای غیر آبستن نیز معنی‌دار بود. افزایش غلظت BUN و کراتینین سرم در شترهای آبستن بالاتر از شترهای غیر آبستن بود. میزان فعالیت GGT در شترهای آبستن بالاتر از شترهای غیر آبستن بود. درآوردن آب انرژی به شترهای ایستگاهی می‌تواند باعث افزایش غلظت کلسیم و فسفر در شترهای آبستن شود.

نتایج نهایی:

پارامترهای خونی، شتر تک کوهانه، آبستنی سنگین، متابولیت‌ها

واژه‌های کلیدی: پارامترهای خونی، شتر تک کوهانه، آبستنی سنگین، متابولیت‌ها

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