



Oxidative Stress Biomarkers and Lipid Profile During the Periparturient Period in Dromedary Camels With Ketosis

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ABSTRACT

This work measured the status of oxidative stress (OS) biomarkers during the periparturient period in dromedary camels with ketosis. The Qassim University Veterinary Hospital in Saudi Arabia registered 17 diseased female dromedary camels. They underwent examination because of the gradual decline in body condition during the first three months post-parturition. Ten clinically healthy female dromedary camels were enrolled in this study as controls. For serum harvesting, collected a 7mL blood sample in plain tubes from each camel. Malondialdehyde (MDA) as lipid peroxidation biomarker and stress indicators, including catalase (CAT), Glutathione (GSH), and superoxide dismutase (SOD), were determined in the sera. In addition, lipid profiles that included cholesterol, triglycerides (TG), high-density lipoproteins (HDL), and low-density lipoproteins (LDL), as well as β -hydroxybutyric acid (β HBA), were measured in the same samples. Compared to the values in the controls, the MDA was significantly higher ($P<0.001$) in the diseased group. However, the GSH value was significantly lower in the diseased camels compared to the healthy ones ($P<0.01$). Similarly, the SOD value was lower in the diseased animals than in the healthy camels ($P<0.001$). The β HBA values were significantly higher in the diseased group than in healthy females ($P<0.01$). The cholesterol, TG, and LDL values were more elevated in the diseased group than in the healthy animal group ($P<0.001$). On the contrary, a statistically significant lower HDL value ($P<0.001$) was found in the diseased group compared to the healthy animal group.

Key words: Biomarkers, Camels, Ketosis, Oxidative Stress, Periparturient Period

INTRODUCTION

The periparturient period, 3 weeks before to 3 weeks after parturition, is characterized greatly by the increased rate of disease. The animal experiences a series of nutritional, physiological, and social changes during this period, and is more vulnerable to infectious and metabolic diseases. Successful transition of the animal from the fetal to the neonatal state involves tremendous physiological adaptations on the part of the neonate and the dam. The success or failure of this transition process equally dictates the survival of the offspring and the subsequent recovery of the dam (Tharwat 2020). During the periparturient period, lipolysis in adipose tissue mobilizes fatty acid reserves to meet high energy needs of dairy cows (Zachut and Contreras 2022).

Overproduction of reactive oxygen species (ROS) indicates an imbalance of oxidants/antioxidants as a source of oxidative stress (OS) that can cause cellular and

tissue damage. As in humans, the occurrence of OS in animals may be the consequence of stressful activities such as transport, exercise, and intensive management (Kirschvink et al. 2002). Thus, this imbalance between the activities of generating and scavenging of radicals required for molecular detoxification results in damage to all cell components, including lipids, proteins, and DNA (Kowaltowski and Vercesi 1999; Niki 2009). Heightened ROS generation, an impaired antioxidant system, or the two in combination can lead to OS. Under OS, an uncontrolled ROS attack can modify and denature molecular function and structure, resulting in dysfunction and tissue damage (Vaziri 2008) and subsequently causing disruptions in the normal cellular detoxification or damage-repair mechanisms of the reactive intermediates (Lands et al. 1999; Wang et al. 2022).

The antioxidative status of the body was determined by two mechanisms, the non-enzymatic one (antioxidants, free radical scavengers, transition metal ions, sequester

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transition metal ions, albumins, ceruloplasmin, and metallothioneins). The other was enzymatic mechanisms, both determine the state of oxidative stress (Kleczkowski et al. 2003; Ghaffar et al. 2021) Dangerously reactive intermediates can be generated by the reduction of oxygen as a by-product of normal aerobic metabolism. All cellular macromolecules are threatened by these ROS as well as by others they engender, therefore creating the need for defences. Nucleic acids and proteins suffering from oxidative damage are repaired or recycled by enzymes that form part of these defences. The role played by this oxidative damage in neurodegenerative diseases and in aging is well established (Freidovich 1999).

Intermediates reactive oxygen can be made in various areas of the hepatocytes. In order for the liver to function normally, it is essential that a balance be maintained between free radical reactions and antioxidant activities. Pathological processes upset this balance (Blázovics et al. 1992). The antioxidant system is composed of antioxidant enzymes including superoxide dismutase (SOD), CAT, and glutathione peroxidase, glutathione (GSH), ancillary enzymes (glutathione reductase and S-transferase, in addition to glucose 6-phosphate dehydrogenase), metal-binding proteins (ceruloplasmin, transferrin, and albumin), vitamins (ascorbate, alpha-tocopherol, and beta-carotene) in addition to flavonoids, and urate (Halliwell 1994; Abd Allah et al. 2007; Mahmood et al. 2022). Under several diverse pathological conditions, free radicals generate tissue damage via the general mechanism of lipid peroxidation (Halliwell and Chirico 1993) Malondialdehyde (MDA) is the most extensively applied common biomarker used in biological and medical science for the assessment of lipoperoxidation (Bird and Draper 1994; Suttner et al. 2001; Salar-Amoli et al. 2009; Li et al. 2022). Thus, as MDA is one of the end products of lipid peroxidation, the degree of peroxidation is most frequently determined by evaluating MDA levels (Lata et al. 2004).

A complex relationship occurs between OS and inflammation, with OS considered as a major component involved in the pathogenesis of conditions and diseases of the skin including edema, erythema, wrinkling, hypersensitivity, abnormal keratinization, and cancer (Bickers and Athar 2006; Portugal and Barak 2007). The design of this work was aimed at assessing the status of the OS biomarkers during the periparturient period in dromedary camels with ketosis. It is hoped that ongoing research on these biomarkers will provide insights that increase the understanding of the physiology of this period.

MATERIALS AND METHODS

Ethical approval

Animal Ethical Committee, Scientific Research Deanship in the University of Qassim, Saudi Arabia was approved this study.

Camels, History, Physical Examination, and Blood Sampling

Seventeen female dromedary camels were examined at the Qassim University Veterinary Hospital in Saudi Arabia. They were described for evaluation because of

gradual loss of body condition during the first three months after parturition. During the clinical examination, the overall behavior and physical illness was observed, auscultation of the heart, lungs, rumen, and intestines was done, the heart rate, respiratory rate, and rectal temperature were measured, and finally, swinging and percussion auscultation of both sides of the abdomen and a rectal examination were performed. Ten clinically healthy female dromedary camels were enrolled in this study as controls. A 7mL blood sample was collected in plain tubes from each camel for serum harvesting.

Determination of Stress Biomarkers and Lipid Profile

Levels of serum malondialdehyde (MDA, Elabscience), cholesterol (Quimica Clinica Aplicada, S.A.), triglycerides (TG, Linear Chemicals, S.L.U.), high-density lipoproteins (HDL, Cintronic GmbH), low-density lipoproteins (LDL, TRI-(TRI/5+HDL) and β -hydroxybutyric acid (β HBA, Biochemical Enterprise) as well as glutathione (GSH, Elabscience), and superoxide dismutase (SOD, Elabscience) activities were calorimetrically measured using kits.

Statistical Analysis

Statistical analysis was performed using GraphPad prism 5. Descriptive statistics and simple t test were performed to compare the diseased and normal groups, with $P < 0.05$, $P < 0.01$, and $P < 0.001$ revealing a significant difference.

RESULTS

Fig. 1 shows mean \pm SD values of the MDA (mmol/g Hb) and β HBA (mg/dL) in diseased female camels during the periparturient period compared to controls and are significantly different at $P < 0.0001$ and $P < 0.05$, respectively. Compared to the value of 177 ± 55 mmol/g Hb in the healthy female camels, the MDA was significantly higher (487 mmol/g Hb, $P = 0.0001$) in the diseased group. The β HBA values were significantly higher in the diseased animals than in the non-diseased females (1534 ± 1209 vs. 286 ± 182 mg/dL; $P < 0.05$).

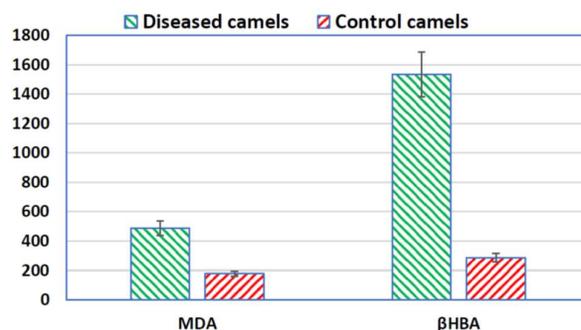


Fig. 1: Mean \pm SD values of the MDA (mmol/g Hb) and β HBA (mg/dL) in diseased female camels (n=17) during the periparturient period compared to controls (n=10) are significantly different at $P < 0.0001$ and $P < 0.05$, respectively.

Fig. 2 illustrate Mean \pm SD values of the GSH (mmol/g Hb) and SOD (U/mg Hb) in diseased female camels during the periparturient period compared to

controls and are significantly different at $P<0.01$ and $P<0.0001$, respectively. The GSH value was lower in the diseased camels than in the healthy ones, with a statistically significant difference (3.46 ± 1.5 vs. 6.02 ± 1.6 mmol/g Hb; $P<0.01$). In a similar manner, the SOD value was lower in the diseased female camels compared to the healthy ones, with a statistically significant difference (5.26 ± 3.2 vs. 10.92 ± 3.9 mmol/g Hb; $P<0.001$).

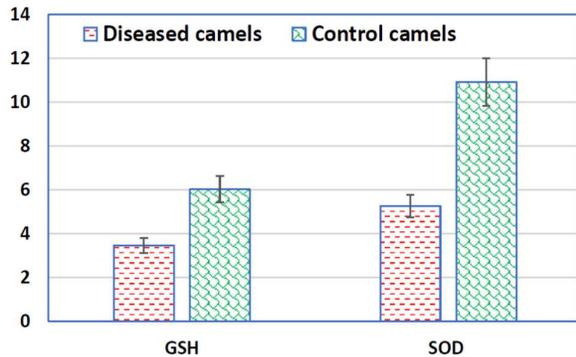


Fig. 2: Mean±SD values of the GSH (mmol/g Hb) and SOD (U/mg Hb) in diseased female camels ($n=17$) during the periparturient period compared to controls ($n=10$) are significantly different at $P<0.008$ and $P<0.0001$, respectively.

Fig. 3 shows mean±SD values of the cholesterol and triglycerides (mg/dL) in diseased female camels during the periparturient period compared to controls and are significantly ($P<0.0001$) different. Fig. 4 clarify Mean±SD values of the high-density lipoproteins (HDL) and low-density lipoproteins (LDL) (mg/dL) in diseased female camels during the periparturient period compared to controls are significantly ($P<0.001$) different. Cholesterol, TG, and LDL values were higher in the diseased group compared to the healthy group (151 ± 15 , 223 ± 20 mg/dL, and 100 ± 19 vs. 108 ± 7 , 139 ± 24 , and 59 ± 16 mg/dL; $P<0.0001$, $P<0.0001$, and $P=0.0002$, respectively). On the contrary, the HDL value was lower in the diseased group compared to the healthy animals, with a statistically significant difference of 7.67 ± 5.9 vs. 36.46 ± 8.8 mg/dL; $P<0.0001$).

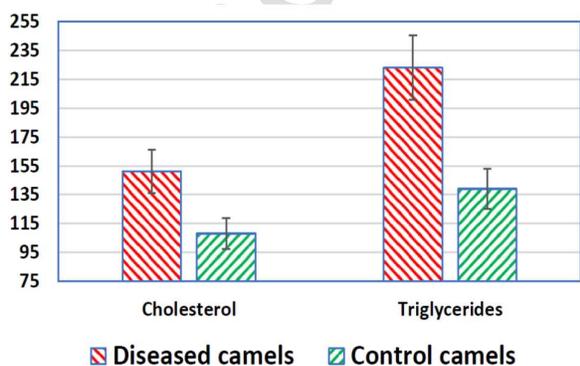


Fig. 3: Mean±SD values of the cholesterol and triglycerides (mg/dL) in diseased female camels ($n=17$) during the periparturient period compared to controls ($n=10$) are significantly ($P<0.0001$) different.

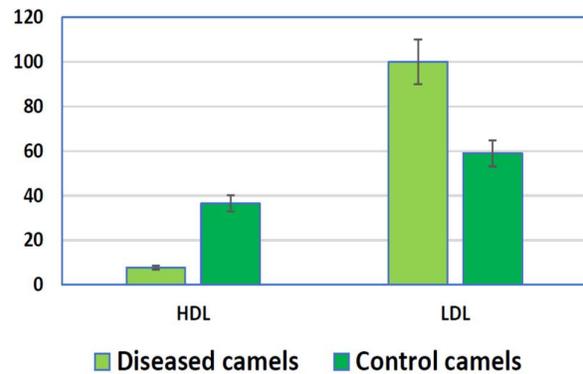


Fig. 4: Mean±SD values of the high-density lipoproteins (HDL) and low-density lipoproteins (LDL) (mg/dL) in diseased female camels ($n=17$) during the periparturient period compared to controls ($n=10$) are significantly ($P<0.0001$) different.

DISCUSSION

During the periparturient period, dairy cattle experience physiological and hormonal changes and severe negative energy balance, followed by oxidative stress. To maintain successful lactation and combat negative energy balance, excessive fat mobilization occurs, leading to overproduction of ROS. Excessive fat mobilization also increases the concentrations of non-esterified fatty acids and β HBA during the periparturient period (Khan et al. 2022). Dairy cows experience increased oxidative stress during periods of transition such as at the cessation of lactation and around the periparturient period, thus increasing disease risk (Strickland et al. 2021). Dairy cattle experience health risks during the periparturient period. The continuous overproduction of ROS during the transition from late gestation to peak lactation leads to the development of oxidative stress.

Oxidative stress is usually considered the main contributor to several diseases such as retained placenta, fatty liver, ketosis, mastitis and metritis in periparturient dairy cattle. The OS is generally balanced by the naturally available antioxidant system in the body of dairy cattle. However, in some special conditions, such as the periparturient period, the natural antioxidant system of a body is not able to balance the ROS production (Xiao et al. 2021). A better comprehension of the redox status (balance between oxidants and antioxidants) during the periparturient period may facilitate the development of management and nutritional solutions to prevent subclinical hyperketonemia and subclinical hypocalcemia in dairy goats (Huang et al. 2021).

Conditions, activities, or events that occur within the body are termed biomarkers because they can indicate physiological or pathophysiological processes (e.g., growth and aging) as well as disease (e.g., heart failure and cardiac damage). Overwhelming change in the two arms of antioxidant either enzymatic or non-enzymatic parameters could be a biomarker to that supports continuation health during the peri-parturient period in dromedary camels with the purpose of diminish the incidence and harshness of diseases and, subsequently, to build up a respectable organization procedure (Ateya et al. 2021).

The biomarkers of stress are used for evaluation of many diseases in camel medicine. For example, the activities of SOD and CAT and reduced glutathione (RGS) levels were significantly lower in camels with paratuberculosis compared to healthy camels. On the contrary, lipid peroxidation was significantly higher, as reflected in higher MDA values in the serum of the infected camels compared to controls (El-Deeb et al. 2014). The activities of SOD, CAT, and RGS were also reduced significantly in camels with trypanosomiasis compared with controls, whereas lipid peroxidation was increased significantly, as revealed by higher MDA values in the serum of these camels compared to healthy controls (El-Bahr and El-Deeb 2016). In camels with sarcoptic mange, concentrations of MDA did not differ in mild cases, but were elevated in moderate and severe cases when compared to control group values. The values of SOD and CAT were significantly higher in mild cases and significantly lower in moderate and severe cases than in the healthy camels. The GSH concentration followed a similar trend, where it was higher in mild and lower in moderate and severe cases compared to the healthy animal values (Saleh et al. 2011). The prognostic and diagnostic significance of OS markers was also studied in camels with urinary tract infection, where CAT, SOD, and GSG activities were decreased in the diseased animals than in the control camel group (El-Deeb and Buczinski 2015; Hussain et al. 2018).

During the periparturient (transition) period, the endocrine status of an animal undergoes more affected changes than at any other time in the cycle of gestation and lactation, in addition to being affected by a reduction in feed intake at a time when the developing conceptus and imminent lactogenesis create an increasing nutrient demand (Drackley 1999). During this transition phase, bovines must adapt to a remarkable and manifold rise in nutrient intake resulting from the lactogenesis needs of the mammary glands, in contrast to the much smaller nutritional requirements of the developing conceptus in late gestation (Tharwat et al. 2012; Tharwat et al. 2015a) This situation is in parallel with various hematobiochemical changes reported as taking place in female dromedary camels in the course of the periparturient period (Tharwat et al. 2015b).

This study was carried out on female camels with ketosis during the first three months postpartum, when their high milk production resulted in a negative energy balance. In periods of food deprivation, ruminants suffer from a breakdown of body tissue, which commonly induces the main energy-producing pathway to shift towards increasing ketone body formation (i.e., β HBA and acetoacetate). However, when food is unavailable, camelids have the ability to utilize free fatty acid and ketone bodies more successfully for their energy and glucose requirements and therefore, do not need to rely entirely on the traditional ruminant biochemical routes (Wensvoort et al 2001). The negative energy balance in the diseased camels was confirmed in this study by the significant elevations in β HBA and by significant increases in cholesterol, TG, and LDL and decreases in HDL compared to the control values. Similar increases in cholesterol and LDL and decreases in HDL were observed

in goats and cows postpartum (Tharwat et al. 2015a; Afzal et al. 2022).

In dromedary camels with a normal periparturient period, it was reported that the levels of MDA did not differ significantly between the prepartum and postpartum periods (Saleh et al. 2021). However, in the present study, the MDA biomarker of lipid peroxidation increased sharply in female camels with progressive weight loss during the three months post parturition ($P=0.0001$). Saleh et al. (2021) observed that SOD activity also increased by 71.7% ($P<0.05$) one-week prepartum and by 57% at parturition. On the other hand, the serum activity values of SOD in this study were lower in the periparturient female camels compared to the healthy ones, with a highly significant difference of $P=0.0001$.

Conclusion

In conclusion, OS biomarkers and lipid profiles measurements might be applied as suggesting biomarkers during the periparturient period in dromedary camels with ketosis. The antioxidant therapy may be valuable in the cure of ketosis in dromedary camels at periparturient period.

Conflict of Interest

The author declares that there is no conflict of interest.

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Uncorrected Proof