Llamas (Lama glama) are no longer considered exotic animals in Europe outside of their natural habitat in South America, so veterinarians are regularly faced with treating llamas or other South American camelids (SAC) like alpacas. In contrast to domestic ruminants, SACs regularly exhibit significant hyperglycemia. Due to a weak insulin response and a slow cellular uptake, glucose levels in SAC often exceed 10 mmol/L. Hyperglycemia can be a stress-related finding, but it can also be associated with serious disease, such as diabetes mellitus, and a poor prognosis for the animal, which was also already studied in detail in companion animals.

In everyday practice, it is not always easy to distinguish whether hyperglycemia is stress induced or whether it is due to pathological changes, like diabetes mellitus. In cats, where stress-induced hyperglycemia plays an important role in veterinary laboratory diagnosis, plasma fructosamine is used to distinguish acute hyperglycemia caused by stress from chronic hyperglycemia in other species, which might be caused by disorders of the glucose metabolism.

**OBJECTIVE**
The objective of this study was to provide orientation values for fructosamine in adult llamas and to characterize relationships with other laboratory and clinical parameters.

**ANIMALS**
Data from 22 healthy adult llamas of both sexes.

**METHODS**
A retrospective study was conducted with the findings of a veterinary herd visit from August 2022. Fructosamine measured from plasma samples was characterized, and its relationships with clinical and laboratory diagnostic data was analyzed using descriptive statistics and correlation analysis.

**RESULTS**
Fructosamine was 311 ± 34 µmol/L (mean ± SD), with a range of 254.8 to 409.2 µmol/L. Males showed significantly higher plasma fructosamine levels than females (P < .05). Plasma fructosamine revealed significant positive correlations with glucose, total protein, and albumin and also with PCV, hemoglobin, calcium, sodium, and selenium. Female llamas revealed further positive correlations with body condition scoring.

**CLINICAL RELEVANCE**
The results of this study can be used as orientation values for fructosamine in llamas. Fructosamine is used to distinguish acute hyperglycemia caused by stress from chronic hyperglycemia in other species, which might be caused by disorders of the glucose metabolism.

**Keywords:** fructosamine, glucose, stress, clinical pathology, South American camelids
overview of the plasma glucose level over the previous 2 to 3 weeks. In contrast to plasma glucose, this parameter is robust against short-term glucose peaks. As plasma fructosamine can be measured by a colorimetric test, which, unlike immunological assays, is inexpensive and robust to species differences, the determination of plasma fructosamine concentration could also be a valuable laboratory diagnostic parameter in llamas. To our knowledge, however, there is little information on fructosamine in llamas.

To obtain preliminary information on this parameter in llamas, we compared plasma fructosamine levels in 22 llamas sampled during a veterinary herd visit with other laboratory and clinical parameters of the animals.

**Methods**

**Herd**

In August 2022, a veterinary herd visit was carried out on a mixed llama and alpaca farm in northeastern Germany. The reason for the visit was the acute death of 5 animals within a few weeks. At the time of the visit, 23 llamas and 9 alpacas were kept on the farm. Intact males were kept on separate pastures from neutered males, females, and crias. The animals underwent a general clinical examination in accordance with the protocol of our clinic, and blood samples (EDTA, Monovette 9 mL K3E; Lithium-Heparin, Monovette 9 mL LH; and serum, Monovette 9 mL Z; all from Sarstedt AG & Co KG) were taken from the jugular vein. Adult animals were fixed in a chute for examination and sampling. Crias were fixed by the animal owner. Because they were used to being handled by people, they were usually quickly captured and well restrained. Detailed information about the herd and the body condition scores (BCS) of the animals was published elsewhere. As a newborn male cria was not sampled at the time of the herd visit, complete data were available from a total of 22 adult llamas (4 intact males, 4 neutered males, 14 females).

The study was approved by the ethics committee of the University of Veterinary Medicine Hannover (approval code: TiHo-REC_14_11_24).

**Clinical examination**

Clinical parameters that were assessed were rectal temperature (°C), as well as heart rate, respiratory rate, and frequency of the contractions of the first compartment (C1 contractions) each (1/min). The previously described gold standard BCS (gsBCS) of the animals was used for the evaluation of the BCS. For interpretation of the clinical parameters, references according to Fowler and Johnson were used: rectal temperature, 37.5°C to 38.9°C; heart rate, 60 to 90/min; respiratory rate, 10 to 30/min.

**Laboratory measurements**

Collection tubes were cooled on ice packs until processing in the laboratory. Lithium-heparin and serum tubes were centrifuged for 30 minutes at 2,000 X g within 5 hours after collection, and the supernatant was transferred to a new container and stored at −20°C until measurements were performed.

Hematological parameters from the EDTA samples and biochemical parameters from the plasma were measured in the clinic’s own laboratory. Hematological parameters were determined using standard manual methods, which were described elsewhere.

Fructosamine concentration (µmol/L) was measured from plasma using a biochemical analyzer (Cobas Mira Plus; Roche Pharma [Schweiz] AG) with a commercial kit (Fruktosamin; Labor + Technik Eberhard Lehmann GmbH) according to the manufacturer’s instructions. The colorimetric method is based on the fact that fructosamine reduces nitro blue tetrazolium to formazan in an alkaline milieu, which is a common method in veterinary laboratory diagnostics. The method was validated 1 to 3 times on each working day with 2 different control sera (Fruktosamin-Kontrolle Level 1 and Fruktosamin-Kontrolle Level 2; Labor + Technik Eberhard Lehmann GmbH). The other biochemical parameters measured in plasma included total protein (g/L), albumin (g/L), glucose (mmol/L), creatinine (µmol/L), urea (mmol/L), calcium (mmol/L), magnesium (mmol/L), phosphate (mmol/L), sodium (mmol/L), potassium (mmol/L), and plasma hemoglobin (Hb; g/L). Those parameters were measured in accordance with the standard procedures of the clinic. Copper (µmol/L) and selenium (µg/L) were measured in serum samples by atomic absorption spectroscopy (AA Spectrometer M Series; Thermo Electron Manufacturing Ltd). For interpretation of the laboratory parameters, reference intervals from Fowler and Zinkl were considered, and trace elements were interpreted according to Stanitznig et al.

Fecal samples were taken from each animal and examined for parasites and interpreted according to Neubert et al.

**Statistical analysis**

The data were transferred to an Excel sheet (Microsoft Corp), and statistical analyses were performed with standard software (SAS Enterprise guide, version 7.1; SAS Institute Inc). Descriptive statistics were expressed as mean, SD, median, minimum, and maximum. All groups were tested for normal distribution using the Shapiro-Wilk test. Data for which the Shapiro-Wilk test revealed P < .05 were not considered to be normally distributed. Differences between male and female llamas, as well as between intact and neutered males, were tested using the t test (if the Shapiro-Wilk test P ≥ .05) or the Mann-Whitney U test (if the Shapiro-Wilk test P < .05). Correlation analysis (Pearson correlation coefficient if the Shapiro-Wilk test P ≥ .05; Spearman rank correlation coefficient if the Shapiro-Wilk test P < .05) was performed to test the relationship between fructosamine and age, rectal temperature, BCS, breath rate, heart rate, C1 contractions, PCV, WBC count, Hb, neutrophil-to-lymphocyte ratio (NLR), lymphocytes, segmented neutrophils, band neutrophils,
metamyelocytes, eosinophils, basophils, monocytes, normoblasts, total protein, albumin, glucose, creatinine, urea, calcium, magnesium, phosphate, sodium, potassium, copper, selenium, and Hb in plasma. A \( P \) value of less than .05 was considered significant. Correlation analysis was interpreted as follows: \( r = 0 \) to 0.1, negligible correlation; \( r = 0.1 \) to 0.39, weak correlation; \( r = 0.4 \) to 0.69, moderate correlation; \( r = 0.7 \) to 0.89, strong correlation; and \( r = 0.9 \) to 1.0, very strong correlation.

Results

Health status of the herd

The animals of the herd were classified as “clinically healthy.” No relevant signs of disease were observed in any of the animals during the clinical examination or after evaluation of the laboratory results. Mild hyperthermia (39.2 °C) was observed in 1 male; 2 llamas revealed mild hypothermia: 1 10-year-old female had a rectal temperature of 37.3 °C and 1 19-year-old female of 36.5 °C. Four llamas revealed bradycardia, and 3 revealed tachycardia. Respiratory rate was above the reference interval in 18 of the 22 animals and reached frequencies up to 80/min. The Hb of 5 llamas and the PCV of only 1 llama were slightly below the reference interval; aberrations in WBC count were not observed in any animal. However, band neutrophils in 14 animals were above the upper reference of Fowler and Zinkl, with the highest value of 0.77 109/L. Total protein was slightly elevated in 8 llamas; albumin was slightly decreased in 1 llama. Two animals had mild hypocalcemia, 9 animals had mild hyponatremia, 1 animal had slightly increased serum copper, and 2 animals had slightly decreased serum selenium values. None of the llamas revealed increased urea or creatinine nor deviations of plasma potassium, plasma phosphate, or plasma glucose. There was no statistical difference between the intact and neutered males in any parameter. Female llamas revealed significantly lower PCV, Hb, basophils, glucose, and selenium than male llamas.

Coccidia oocysts were found in low numbers in 10 llamas and moderate numbers in 2 llamas. Seven llamas revealed low-grade infestation with gastrointestinal nematodes. *Eimeria macusaniensis* was detected in the feces of 3 llamas.

---

Figure 1—Plasma fructosamine of 22 healthy adult llamas of both sexes examined in August 2022 from a herd in northern Germany. The scatter plots indicate fructosamine in relation to (A) age, (B) plasma glucose, (C) total protein, and (D) albumin. Each circle represents the results of a single animal; the line represents the regression line. Although the correlation of fructosamine and age was negligible, there were moderate positive correlations between fructosamine and glucose, total protein, and albumin.
Fructosamine

The mean plasma fructosamine concentration of the 22 llamas in this herd was 311.0 (34.0) µmol/L (mean [SD]) and ranged from 254.8 to 409.2 µmol/L. Male llamas had significantly higher plasma fructosamine (333.7 [40.7] µmol/L) than the females (298.0 [21.9] µmol/L; P < .05). Correlation analysis revealed a strong positive correlation between fructosamine and Hb (r = 0.82; P < .001) and moderate positive correlations between fructosamine and PCV (r = 0.63; P < .001), glucose (r = 0.58; P < .01) (Figure 1), total protein (r = 0.54; P < .01) (Figure 1), albumin (r = 0.54; P < .01) (Figure 1), calcium (r = 0.45; P = .04), sodium (r = 0.53; P = .01), and selenium (r = 0.54; P = .01). No statistically significant correlations with fructosamine were found for age (Figure 1) or the clinical parameters rectal temperature, heart rate, respiratory rate, and frequency of C1 contractions in this population. However, correlation of BCS and plasma fructosamine revealed a statistical trend (r = 0.42; P = .06) in the entire population. When dividing the herd into sexes, there was a moderate positive correlation between plasma fructosamine and BCS in female llamas (r = 0.62; P = .03). A detailed overview of the results of the clinical and laboratory diagnostic findings in this herd can be found in Supplementary Tables S1–S5.

Discussion

To our knowledge, these are the first data on plasma fructosamine in llamas. According to Dawson et al,14 the reference interval for plasma fructosamine in alpacas is 252 to 425 µmol/L,14 which is similar to our findings. In that study by Dawson et al,14 74 alpacas from 5 different farms in New York were included, and parameters were measured in both serum and plasma. Although the reference interval for serum fructosamine was given as 251 to 431 µmol/L and was therefore almost identical, there was a statistical significant difference in the medians, with lower values in plasma compared to serum.14 In a case report on an alpaca with hypercholesterolemia, serum fructosamine was reported to be 368 µmol/L, whereas the serum fructosamine of 3 healthy animals used for comparison had a range of 288 to 409 µmol/L.15

Compared to reference intervals or orientation values from other species, like cats,21 dogs,23 cattle,20 or donkeys,21 the determination of fructosamine in SAC reveals higher values. Sex differences, with higher fructosamine in males compared to females, are already known for alpacas14 and have also been described for other species, like cats, Rhesus macaques, or foxes.32 This sex difference can be explained by a difference in plasma glucose levels. Male llamas in our study had a significantly higher plasma glucose level than female llamas, whereas no sex difference was found for total protein or albumin. Higher glucose levels in male compared to female llamas have also been reported before by Hengrave-Burri et al33 and Gallelli et al.34 In contrast to our data, Hengrave-Burri et al33 also found higher albumin in males in their studies on a larger number of animals (33 male and 79 female llamas), which could also contribute to the increased fructosamine in male llamas. Lower Hb in female llamas has also been previously described,35 but no sex-specific differences in basophils or selenium in llamas were found in the literature. However, Husakova et al35 found no differences between male and female alpacas with respect to selenium in whole blood.

We further detected an influence of BCS on fructosamine in female llamas. This correlation can probably be explained by the fact that albumin also shows a significant positive correlation with the BCS of the animals. An influence of BCS on fructosamine has also been described in other species; cats and cattle with higher BCS also have higher fructosamine concentrations than those with lower BCS.36,37 However, the age of the animal does not seem to have an influence on fructosamine in llamas, which is also in line with the results of Gilor et al,36 who investigated fructosamine in cats. The significant positive correlations of fructosamine with glucose, total protein, and albumin can be explained by the fact that fructosamine is a product of glucose and plasma proteins, of which albumin is the largest fraction.12 Although stronger correlations of fructosamine with total protein (r = 0.81) and albumin (r = 0.75) have been reported for diabetic humans,38 Kawamoto et al39 also found lower correlations for total protein (r = 0.24) in their study of clinically healthy dogs. The correlation for fructosamine and albumin was somewhat stronger (r = 0.62) than in the llamas presented here. Dogs with hypoalbuminemia showed a stronger correlation of albumin and fructosamine (r = 0.71) than the dogs with normal albuminemia (r = 0.17). Such a comparison cannot be made for the llamas as only 1 animal exhibited low-grade hypoalbuminemia, but fructosamine in this animal, at 279.7 µmol/L, was the third lowest of the 22 llamas examined.

However, positive correlations of fructosamine with PCV, Hb, calcium, and selenium remain unclear and require further investigation. To our knowledge, there are no such findings in the literature on other species. The findings on the positive correlation between fructosamine and selenium appear contradictory to the results of Alehagen et al,40 who found that after 42 months of selenium supplementation, fructosamine levels in humans were significantly lower than those of the placebo group. Although elevated fructosamine levels have been described in nondiabetic humans suffering from iron-deficiency anemia,41 a comparison does not seem appropriate here as the llamas did not have pronounced anemia.

An association with hyperproteinemia due to endoparasites seems unlikely as the examined herd had no or only very low levels of gastrointestinal nematodes and did not reveal hypoproteinemia at the point of sampling.

On the basis of the clinical and laboratory diagnostic findings, we assume that the animals of this population were healthy. The herd visit took place on a warm summer’s day with temperatures of up to 36 °C. Hyperthermia, tachycardia, and tachypnea
that occurred in some cases were interpreted as a reaction to heat and the fixation as individual animals were defensive. Deviations in some parameters in single animals were considered irrelevant findings. In comparison to the reference intervals by Fowler and Zinkl,24 many animals had slightly increased band neutrophils. If, for example, the reference intervals from van Houten et al42 or Garry et al43 were used here, only 6 of 22 animals would have slightly elevated band neutrophil values. The deviations of the macro and trace elements from the reference intervals were only minimal; we therefore consider these values to be clinically irrelevant. The endoparasites found in some animals are to be regarded as incidental findings and occur regularly in SAC kept in Germany.2 The diagnosis of the deceased animals from this flock was suspected to be acute clostridiosis after all the findings had been processed.

The number of animals was small; the measurement of fructosamine took place in retrospect. Thus, the values do not represent reference values but can be used for orientation. The results of glucose degradation of approximately 5% per hour can be assumed.44 Five animals revealed plasma Hb > 0.3 g/L and could be classified as hemolytic,45 but there were no numerical aberrations of the measured values compared to the other animals.

Fructosamine reflects the glucose level over several days and is also closely related to plasma glucose, total protein, and albumin in llamas. This could be used in the diagnosis of diseases of glucose metabolism in this species. In addition to fructosamine, glycated Hb has been established in companion animals. This parameter provides an overview of the plasma glucose level over the last 2 to 3 months.46 Glycated Hb could also play a role for SAC in the future.

Acknowledgments

The authors gratefully acknowledge the help of Stefan Germann, Nina Ossowski, and Anna Trojakowka for the good cooperation and help with the examination of the animals. They also acknowledge the help of Frances Sherwood-Brock, English Editorial Office, University of Veterinary Medicine Hannover, Foundation, for proofreading the manuscript to ensure correct English. We acknowledge financial support by the Open Access Publication Fund of the University of Veterinary Medicine Hannover, Foundation.

Disclosures

The authors have nothing to disclose. No AI-assisted technologies were used in the generation of this manuscript.

Funding

The authors have nothing to disclose.

ORCID

M.G. Wagener https://orcid.org/0000-0003-3366-8579

References


20. Wagener MG, Neubert S, Punsmann TM, Wiegand SB, Ganter M. Relationships between body condition score (BCS), famacha-score and haematological parameters in alpacas (Vicugna pacos), and llamas (Lama glama) presented at the veterinary clinic. Animals. 2021;11(9):2517. doi:10.3390/ani11092517


Supplementary Materials

Supplementary materials are posted online at the journal website: avmajournals.avma.org.