DOI: 10.1638/2020-0064 *Journal of Zoo and Wildlife Medicine* 53(1): 000–000, 2022

COMPARISON OF DIAGNOSTIC PREDICTORS OF NEONATAL SURVIVABILITY IN NONDOMESTIC CAPRINAE

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Abstract: This retrospective study evaluated whether six methods (glutamyltransferase, glutaraldehyde coagulation test, sodium sulfite precipitation test, total serum protein, glucose, and fibrinogen) used to assess passive transfer status in ruminants were predictive of survival of nondomestic Caprinae neonates in a zoological collection. A total of 184 neonates from 10 nondomestic Caprinae species had one or more testing methods performed within 7 d of birth. Results of each test were compared with the clinical condition (alive or dead) at 7, 30, and 90 d of age. Total protein (TP) results were not considered for statistical significance in this study. No statistical correlations between results of the serum gamma glutamyltransferase (GGT), glutaraldehyde coagulation test, or sodium sulfite precipitation test (BOVA-S) and survival at any age were found. A higher glucose level within 7 d of birth was associated with a greater probability of survival. Fibrinogen levels were found to have a strong negative association with survival at 30 and 90 d. Increased glucose concentration was negatively associated with the probability of an infectious cause of mortality and the need for medical intervention. In contrast, increased fibrinogen levels were associated with higher probabilities of infectious death and the need for major medical care. Neonates who were confirmed to have nursed had a lower likelihood of requiring major medical intervention. These findings suggest that glucose and fibrinogen levels are better predictors of neonatal survival in nondomestic Caprinae when compared to the other three tests reviewed in this study. Using survival as an indicator of adequate passive transfer in this group of neonates failed to identify a gold standard of diagnosis of failure of passive transfer, so more than one diagnostic test should be utilized.

INTRODUCTION

Postnatal survival of ruminant neonates is affected by adequate colostrum consumption because colostrum contains immunoglobulins (Ig) the neonate is not exposed to prior to parturition because of placental anatomy.[4,5,13] The amount and timing of Ig consumption is critical for proper neonatal immune function.[24] The failure to absorb sufficient Ig results in inadequate immunity in early life, which predisposes the neonate to infections, sepsis, and death.[7,8,12,16] This phenomenon is known as failure of passive transfer (FPT).

Nondomestic ruminant neonates that do not absorb the dam's colostrum can also suffer from FPT. However, diagnosing FPT in nondomestic species can be challenging. Detection of failure of passive transfer has long been performed in domestic ruminant neonates to measure the exact quantity of Ig present by using rapid detection assays such as radial immunodiffusion (RID) and enzyme-linked immunosorbent assays.[4,5,7,23,24] However, their use in nondomestic ruminants is limited because of the lack of species-specific antibody tests and reference intervals. The absence of a validated gold standard method of detection of FPT in nondomestic ruminants, including Caprinae species, results in various unverified methods being used to attempt to identify cases of FPT. Because of the lack of a single ideal FPT testing method, other less-specific techniques have been utilized to aid in detection of individual survivability. These biological testing methods, which have been used to detect FPT in other ruminant species, include total protein refractometry, zinc sulfate turbidity, sodium sulfite precipitation test, serum electrophoresis, and glutaraldehyde coagulation.[6,11,12,17,18,21–24] Because each diagnostic value is poorly understood in nondomestic Caprinae, the tests have been used inconsistently and in different combinations to support a diagnosis of FPT.[12] The more commonly utilized biological tests in a clinical setting for Caprinae at the San Diego Zoo Safari Park (SDZSP) and San Diego Zoo (SDZ) are serum gamma-glutamyltransferase (GGT) activity, glutaraldehyde coagulation, sodium sulfite precipitation test

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(BOVA-S), total protein (TP), glucose, and fibrinogen concentrations.

The reliability of detection of FPT with these tests is variable, which can delay timely intervention in affected individuals. This can lead to inefficiency in management and treatment of these individuals and possible mortality. Early detection of FPT could lead to faster medical intervention (e.g., administration of supplemental colostrum) and may lead to an overall decrease in neonatal mortality of endangered Caprinae species. FPT is seen as a gauge for predictability of calf health and anticipation of survivability.[8] The inability to identify cases of failure of passive transfer in nondomestic Caprinae species has led to increased resource use, expenses, and morbidity and mortality rates in zoological collections.[12] The objective of this retrospective study was to evaluate the potential of several diagnostic tests of FPT and other parameters to predict neonatal survival in nondomestic Caprinae within a zoo collection.

MATERIALS AND METHODS

Medical record review

Ten nondomestic Caprinae species over a period of 29 yr from the SDZSP and the SDZ were included in the study. A total of 184 neonates of these species had one or more testing methods performed within 7 d of birth (Table 1). Each individual received a neonatal exam within the first week of life, which included a physical examination, sex verification, blood collection, and permanent identification. All blood collected was analyzed by the SDZSP or the SDZ clinical laboratories and included a complete blood count, standard serum biochemistry panel, glutaraldehyde coagulation test, and sodium sulfite precipitation test (BOVA-S). Blood laboratory tests were run within 4 h of collection.

Hematology analyzers used over the course of this study included Baker 9000, MS9-5 Malet-Schloesing, and Horiba ABX PDX 120. Chemistry analyzers used during the time frame of this study included Cobas Mira (wet chem), SDI CA 480 (wet chem), and Horiba Petra C 400 (wet chem). The glutaraldehyde coagulation testing method used at SDZSP and SDZ added 200 µl of serum to 20 µL of 10% glutaraldehyde solution. The results were time dependent, with positive being complete coagulation, or negative results being no change or incomplete coagulation found before or at 60 min. The time to reach a positive result was recorded for each individual. BOVA-S was identified as positive or negative result using an aliquot of 0.1 ml of serum with a commercially available sodium sulfite test (Bovas-S, VMRD, Pullman, WA 99163, USA). Glucose, GGT, and TP values were analyzed using ABX Pentra CP (Equipment: Glucose HK CP, GGT CP, or TP 100 CP). This method determines TP in serum by colorimetry. The authors elected to place TP into three categories, high (>8 g/dl), normal (6–8 g/dl) and low (<6 g/dl). Fibrinogen analysis tested the individual's serum fibrinogen by a heat precipitation method. Two EDTA whole blood tubes were centrifuged. One was placed at temperatures between 56 and 58°C for 4 min. The heated tube was then recentrifuged, allowing the fibrinogen to precipitate. Fibrinogen was calculated as the difference between the two total protein readings. No ranges for fibrinogen were created. The numerical values of fibrinogen were evaluated for significance in the logistic regression. Numerical results were identified for CBC, biochemistry panel, and GGT tests. ?1

Medical records of all Caprinae born at the SDZSP between May 1988 and September 2017 were evaluated. The SDZ Cretan goats' data were collected from a previous study in 2005.[12] Each individual record was assessed for species, sex, birth date, date of neonatal exam and blood collection, physical exam abnormalities, nursing observations, laboratory tests (Table 1), medical intervention, treatment, and clinical outcome. Visual observation of nursing was divided into confirmed nursing from the dam or from a colostrum supplementation, or suspected nursing from the dam, not observed by keepers and not identified in the record. These observations were performed prior to diagnostic testing. The decision to give colostrum replacer was made if the individual required hand-rearing. Rearing of the individual after the neonatal exam was identified as either assisted rearing or dam rearing. First, the survival of the neonate at days 7, 30, and 90 following birth was evaluated. This identified death or life at each time point. Next, the clinical intervention required for each individual was evaluated within 7 d of the initial neonatal exam. The individuals were placed into either "minor intervention" or "major intervention" categories. The minor intervention individuals required either no medical follow-up after their neonatal exam or had a singular follow-up exam for minor problems, including short-term antibiotic use, single dipping of the umbilicus, single subcutaneous injections (e.g., dextrose, fluids, and antibiotics), single tube feeding, simple glucose recheck,

Table 1. Individual species' study population and diagnostic modalities performed for various Caprinae species within 7 d of birth.[a]

Species	*N*[b]	GGT	Glutaraldehyde	BOVA-S	Glucose	Fibrinogen	WBC/RET/HCT	TP
Nubian ibex (*Capra nubiana*)	46	28	28	18	29	28	42	43
Turkomen markhor (*Capra falconeri*)	9	5	7	4	5	6	7	7
Armenian mouflon (*Ovis gmelini gmelini*)	10	10	6	4	10	10	10	10
Chinese bharal (*Pseudois nayaur*)	2	2	2	1	2	1	2	2
Desert bighorn (*Ovis canadenis*)	6	6	5	2	6	6	6	6
Sudan barbary (*Ammotragus lervia*)	34	31	32	3	33	33	33	33
Alpine ibex (*Capra ibex*)	4	3	1	3	3	4	4	4
West Caucasian tur (*Capra caucasica*)	5	3	1	4	5	4	4	4
Transcaspian urial (*Ovis gmelini vignei*)	23	22	21	2	23	22	22	22
Cretan goats (*Capra aegagrus cretica*)	45	45	45	0	45	45	45	45
Total	184	155	148	41	161	159	175	176

[a] GGT, serum gamma-glutamyltransferase; glutaraldehyde, glutaraldehyde coagulation test; BOVA-S, sodium sulfite precipitation test; WBC, individual white blood cell counts; RET, reticulocyte count; HCT, hematocrit found from same machine, which identified WBC; TP, total protein.
[b] Total population for each species in the present study.

fracture repair, worn hooves, long umbilicus, or a transient heart murmur. Major intervention individuals required major medical care and were hospitalized, received a plasma transfusion, died naturally, or were euthanized. All individuals that died or were euthanized had gross necropsy reports reviewed for the presence of milk in the abomasum and for postmortem gross and histological findings that would indicate an infectious or noninfectious cause of disease or death.

Statistical analysis

Association between BOVA-S and clinical condition (alive or dead) at the end of the observation period was investigated using Fisher's exact tests. Other predictors of survival at ages 7, 30, and 90 d were examined using logistic regression, where model fitting was performed via generalized estimating equations in order to control for the correlation of longitudinal responses within subjects.[2] Statistical significance was evaluated using these results, but trend analyses separated by age were also compared to study the changes in predictor effects over time (see Fig. 1). In order to obtain a more nuanced picture of survival beyond just life and death, subanalyses for death by infectious causes and the need for major medical intervention were also conducted with logistic regression. Factors considered were sex, weight, white blood cell count, GGT, nursing prior to neonatal exam, blood glucose, fibrinogen levels, and glutaraldehyde test results. The ranges for TP were created to perform a descriptive analysis. The logistic regression was modeled using the $n = 119$ subjects for which each of these measurements was recorded. From the 184 individuals investigated in this study, 65 had missing values of either weight, white blood cell count, GGT, fibrinogen, glucose, or TP. BOVA-S was not included in the model because the sodium sulfate precipitation test was only conducted for 41 subjects. Including BOVA-S would limit the logistic regression to only 41 observations and severely deflate statistical power. A descriptive comparison of rates across levels was performed for nursing, transfusions and total protein, which were not considered for significance and require more nuanced investigation in future research. Values of $P < 0.05$ were considered statistically significant. Statistical modeling was conducted in R, and plots were created using ggplot2.[19,25]

RESULTS

Survival was studied by recording the status of each subject (alive or dead) at ages 7, 30, and 90 d. Of the $n = 184$ total neonates observed, 157 (85.3%) survived to 7 d, 147 (80%) to 30 d, and 143 (77.7%) to 90 d. For the $n = 41$ subjects who were administered a BOVA-S test, no association between test results and survivability at the end of the observation period was found ($P > 0.9$). Similarly, for the subjects who had the glutaraldehyde coagulation test, there was no association between test results and survival ($P = 0.74$). Time to a positive glutaraldehyde coagulation test result was also considered but was not found to predict viability ($P = 0.68$).

For the $n = 119$ neonates who were administered all other tests, higher blood glucose levels were associated with a greater probability of

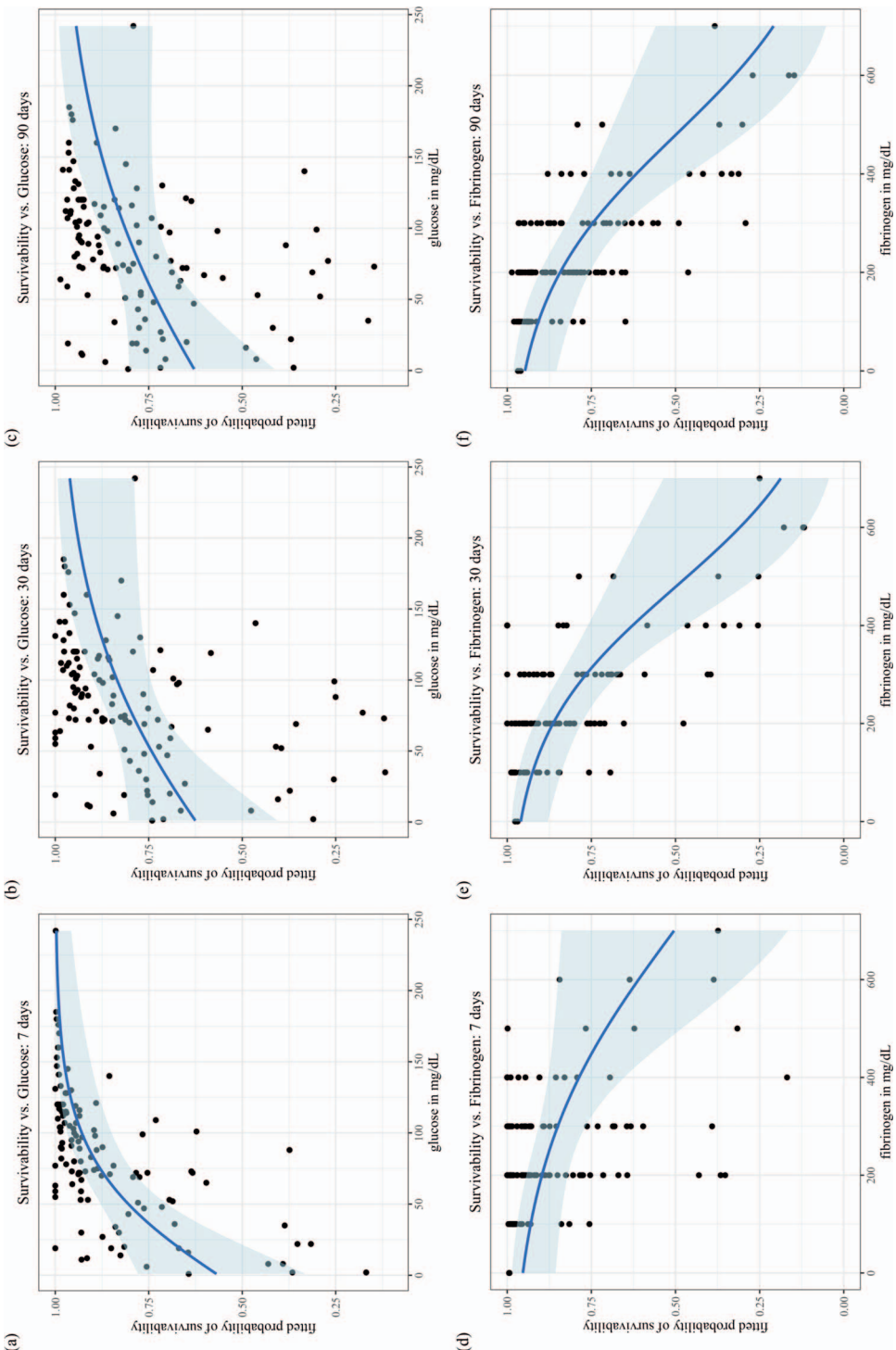

Figure 1. Fitted probabilities of neonatal Caprinae survival vs. (a)–(c) glucose and (d)–(f) fibrinogen levels, separated by age. The fitted curves indicate that survivability rises with increased glucose levels and falls with increased fibrinogen levels. Notice the magnitudes of these effects (reflected in the steepness of the fitted curves) attenuate over time for glucose, but become more pronounced for fibrinogen. (a) Fitted probability of neonatal survivability at 7 d of age and glucose level at neonatal exam; (b) fitted probability of neonatal survivability at 30 d of age and glucose level at neonatal exam; (c) fitted probability of neonatal survivability at 90 d of age and glucose level at neonatal exam; (d) fitted probability of neonatal survivability at 7 d of age and fibrinogen level at neonatal exam; (e) fitted probability of neonatal survivability at 30 d of age and fibrinogen level at neonatal exam; and (f) fitted probability of neonatal survivability at 90 d of age and fibrinogen level at neonatal exam.

Table 2. Effects of predictors on overall survival, infectious death, and medical intervention in Caprinae species. Effects indicate the resulting change in the log–odds of the outcome based on a one-unit change in the predictor. Standard errors are displayed in parentheses and *P*-values less than 0.05 were considered significant. A positive effect corresponds to a positive association between the predictor and the outcome variable, and a similar statement is true for negative values. Taking survival as an example, a higher level of glucose was associated with greater odds of survival. Specifically, the odds of surviving increase by a factor of $e^{0.0161} \approx 1.0162$ for every additional mg/dl of blood glucose at birth. Each Caprinae neonate was identified as deceased or alive at each time interval since day of birth. These days may be +/− 1 d of birth because of finding neonates and uncertain time of birth over the past day. All neonates for which survival was unknown were not included.[a]

	Survival		Infectious death		Intervention	
Factor	effect (SE)	*P*	Effect (SE)	*P*	Effect (SE)	*P*
Male	−0.5925 (0.5821)	0.154	1.1181 (1.0672)	0.295	0.4731 (0.6098)	0.438
Weight	0.3147 (0.3848)	0.207	0.0441 (0.5642)	0.938	−0.4942 (0.4431)	0.265
WBC/RET	−0.0013 (0.0593)	0.412	0.0008 (0.0079)	0.992	0.0673 (0.0709)	0.342
GGT	−0.0010 (0.0009)	0.116	0.0007 (0.0013)	0.615	−0.0014 (0.0012)	0.258
Confirmed nursing	0.6502 (0.7010)	0.176	0.9612 (1.1047)	0.384	−1.384 (0.7797)	**0.076**
Glucose	0.0161 (0.0069)	**0.010**	−0.0330 (0.0141)	**0.020**	−0.0406 (0.0093)	≈**0.000**
Fibrinogen	−0.0054 (0.0023)	**0.008**	0.0073 (0.0032)	**0.023**	0.0062 (0.0029)	**0.032**
Glutaraldehyde (+)	−0.1986 (0.6347)	0.377	0.9660 (1.0620)	0.363	0.1712 (0.6637)	0.797

[a] WBC, individual white blood cell counts; RET, reticulocyte counts; GGT, serum gamma-glutamyltransferase.

survival across all ages ($P = 0.010$). For approximately every additional 25 mg/dl of blood glucose present at the time of the neonate exam, the odds of surviving to 7 d of age increase by approximately two-fold. Mean glucose was 86.62 mg/dl with a 46.15 mg/dl standard deviation (SD); mean fibrinogen was 259.7 mg/dl with a 138.76 mg/dl SD. Trend analysis revealed the effect of neonatal glucose levels on survival weakens as age increased to 30 and 90 d (Fig. 1). The odds of surviving to these ages increased by factors of 1.4 and 1.3, respectively, per each additional 25 mg/dl of glucose.

In contrast to glucose, increased fibrinogen levels were generally associated with a lower probability of survival ($P = 0.007$). The negative effect is not as pronounced at the age of 7 d; rather it emerged as a stronger negative association with survival at 30 and 90 d of age (Fig. 1). For every additional 90 mg/dl of fibrinogen present at the neonate exam the odds of surviving to 30 d of age were decreased by half. A similar statement was true for viability at 90 d. Other covariates were not associated with survival at the evaluated ages (Table 2).

Approximately 7.6% of all Caprinae died of an infectious cause. Increased levels of glucose at exam were negatively associated with the probability of infectious death ($P = 0.020$; Fig. 2), whereas increased levels of fibrinogen were associated with greater risk of infectious death ($P = 0.023$; Fig. 2). For approximately every additional 95 mg/dl of fibrinogen in serum during the neonate exam, the odds of infectious mortality doubled. Additionally, over 50% of neonates with fibrinogen levels at or above 600 mg/dl died of infectious causes. Other tests evaluated (glutaraldehyde coagulation test, glutamyltransferase, and BOVA-S) were not found to have significant associations with the probability of infectious death (Table 2).

Major medical intervention was performed in 26.9% (32/119) of neonates that had complete neonatal testing (except BOVA-S; Table 3). The need for major medical intervention was made based off of clinician discretion. Individuals who received medical intervention had lower survival rates at age 90 d compared to those who did not (50.0% vs. 88.5%, $P < 0.001$). Similarly, infectious death rates were higher among individuals who received intervention (18.8% vs. 3.4%, $P = 0.008$). A comparison of survival, infectious mortality, and intervention can be seen in Table 3. Clinical bias for requirement of major medical intervention was not factored into this study. It is possible that intervention was needed for some individuals that did not receive it or was not necessary for all neonates that did.

Subjects with higher glucose levels generally required intervention at lower rates. The odds of intervention were approximately 50% lower for every 15 mg/dl of glucose found in serum ($P < 0.001$; Fig. 3). Individuals who were confirmed to nurse received major medical intervention at much lower rates than those who were not confirmed to have nursed (10.3% vs. 35%, $P = 0.042$). Fibrinogen levels were higher in neonates that received medical intervention. For every

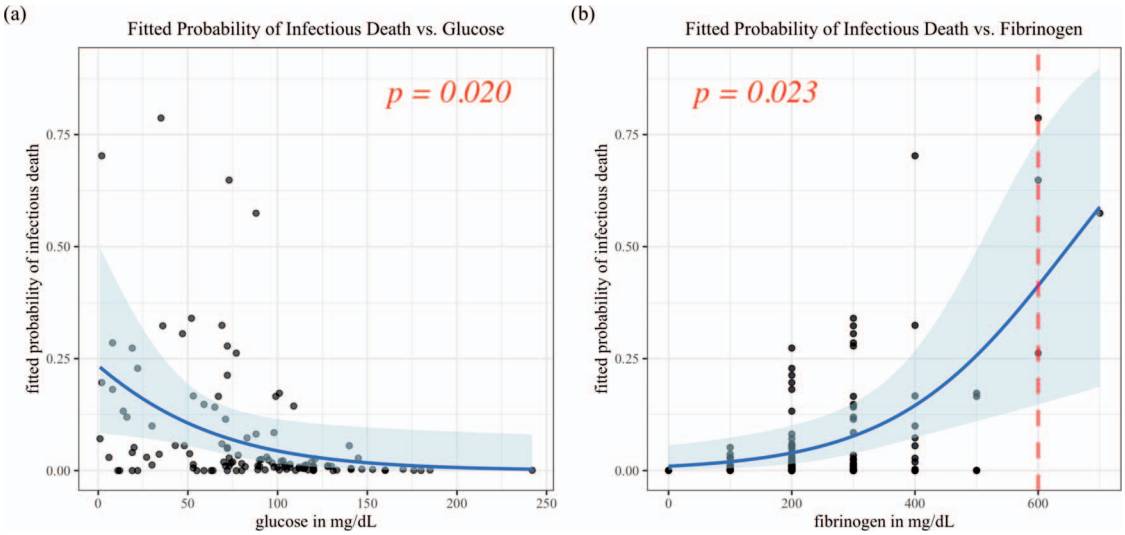

Figure 2. Fitted probabilities of neonatal Caprinae infectious mortality by age 90 d vs. (a) glucose and (b) fibrinogen levels at neonatal exam. The fitted probabilities illustrate the chances of death due to infection decrease as glucose increases, but increase with higher fibrinogen levels. The vertical dashed red line indicates the fibrinogen level above which more than 50% of neonates died. *P*-values correspond to the effects of glucose and fibrinogen on infectious death. *P*-values less than 0.05 were considered significant. (a) Fitted probability of infectious mortality by age 90 d and glucose level at neonatal exam; (b) fitted probability of infectious mortality by age 90 d and fibrinogen level at neonatal exam.

additional 110 mg/dl of fibrinogen present at neonate exam, the odds of intervention doubled ($P = 0.032$; Fig. 3).

Table 4 provides a comparison of survivability and infectious mortality rates based on provided plasma transfusions ($n = 15$), nursing behavior ($n = 184$) and TP levels ($n = 175$). The authors elected to group TP into the three categories including less than 6 g/dl, 6–8 g/dl, and greater than 8 g/dl. Individuals in the low category had an average TP of 4.74 g/dl with standard deviation of 0.63 g/dl and total range of 3.3–6 g/dl. The individuals with normal values within the study's range had an average TP of 6.70 g/dl with standard deviation of 0.38 g/dl and a range of 6.1–7.5 g/dl. The individuals within the higher category had a mean of 24.20 g/dl with a standard deviation of 22.3 g/dl and range from 8.4 to 40.0 g/dl. The majority of subjects (87.4%) had TP levels in the low range. A descriptive comparison of rates across TP levels was provided for completeness.

DISCUSSION

This study evaluated the potential of several diagnostic tests of FPT including GGT, glutaraldehyde coagulation, BOVA-S, glucose, and fibrinogen to predict neonatal survival in nondomestic ruminant species of the family Caprinae within a zoo collection.

Serum GGT is an active enzyme found following consumption of colostrum in domestic animals.[4] An increased serum GGT is assumed to indicate an adequate amount of colostrum consumption. Serum GGT testing method is acceptable for assessing passive transfer in domestic neonatal Caprinae species, specifically lambs.[1,4,12] There is supportive literature indicating GGT is a positive predictor for neonatal viability in greater

Table 3. Comparison of rates and predictors of survival (age 90 d) across levels of major medical intervention in Caprinae sp. The counts of neonates provided in parentheses following the rates.

	Total N	Survival rate, % (n)	Infectious death rate, % (n)	Confirmed nursing rate, % (n)	Mean glucose level (mg/dl)	Mean fibrinogen level (mg/dl)
Intervention	32	50.0 (16)	18.8 (6)	12.5 (4)	49.4	278.1
No Intervention	87	88.5 (77)	3.4 (3)	40.2 (35)	97.7	232.2
P-value		**≈0.000**	**0.008**	**0.004**	**≈0.000**	0.145

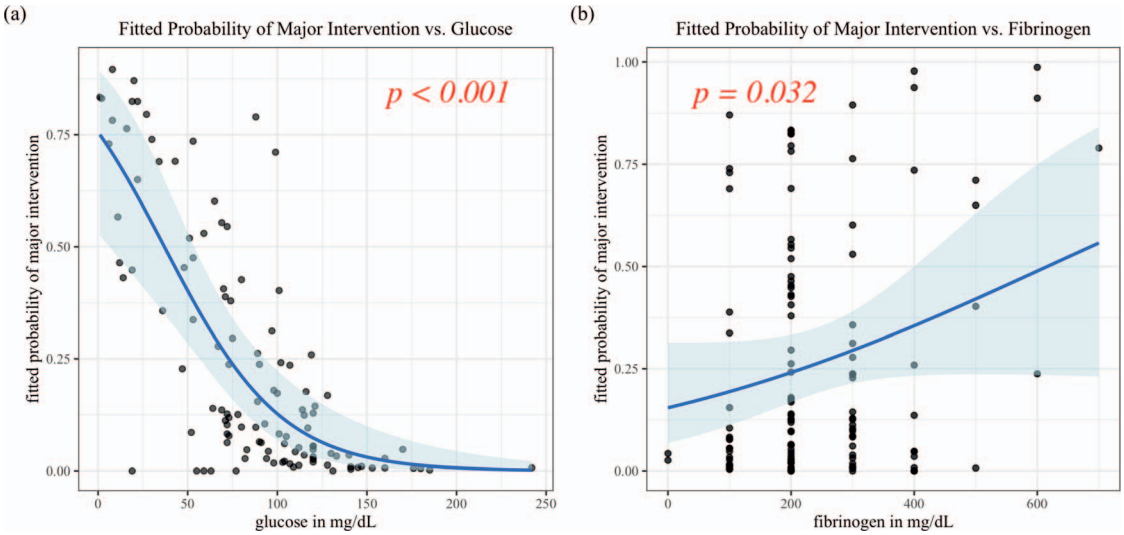

Figure 3. Fitted probabilities of major medical intervention vs. (a) glucose and (b) fibrinogen levels at neonatal exam. The fitted probabilities illustrate that the likelihood of requiring medical intervention decreases as glucose increases, but increases with higher fibrinogen levels. *P*-values correspond to the effect of glucose and fibrinogen on needing intervention. *P*-values less than 0.05 were considered significant. (a) Fitted probability of major intervention by age 90 d and glucose level at neonatal exam; (b) fitted probability of major intervention by age 90 d and fibrinogen level at neonatal exam.

Table 4. Percentage of neonatal Caprinae survival and infectious mortality across plasma transfusion status, nursing, and total protein levels as measured by colorimetry.

Individual neonates and levels	N[a]	Survival rate (%) 7 d	30 d	90 d	Infectious mortality rate (%)
Transfusion					
Received	15	73.3	60.0	60.0	6.7
Not received	120	83.3	77.5	74.2	10.0
Nursing					
Observed[b]	52	90.4	82.7	76.9	7.7
Suspected[c]	17	88.2	88.2	82.4	5.9
Unknown	115	82.6	77.4	77.4	7.8
Total protein[d]					
High	2	100.0	100.0	100.0	0.0
Normal	20	95.0	95.0	90.0	0.0
Low	153	85.0	78.4	76.5	7.8

[a] Total population for all Caprinae in the present study.
[b] Observed; individuals were identified as actively consuming from dam by SDSPZ staff or given replacer by staff. The decision to give colostrum replacer was made if the individual required hand-rearing. This decision was made prior to diagnostic testing.
[c] Suspected; staff saw attempt to nurse but unsure if any substance was received. All unknown to nurse were not considered in this comparison.
[d] High (TP > 8 g/dl), normal (TP = 6–8 g/dl), and low (TP <6 g/dl).

kudu, gazelles, muntjac, and springbok.[10,12,22] The results of this test are fast, inexpensive, and do not appear to be affected by dehydration, making this method a practical choice for detecting failure of passive transfer.[4,12,22] However, GGT results did not correlate with neonatal viability in Cretan goats, and there is a lack of research investigating this method in other species in this Bovid subfamily.[12] In this study, GGT was not a predictor of neonatal survival in nondomestic Caprinae. Similar to domestic calves, there is a possibility that serum GGT values have little to no association with the amount of IgG in the colostrum consumed.

The glutaraldehyde coagulation test utilizes serum-clotting time to evaluate hypogammaglobulinemia, which is used as an indicator of FPT in domestic ruminant species.[3,4,22] This testing method has been shown to identify transfer of maternal antibodies to neonates in nondomestic ruminants species including giraffe, banteng, American bison, and Congo buffalo.[15,18,20] The test is inexpensive and has provided rapid screening in a zoo or field scenario.[15] However, the success of this testing method compared to survivability specifically for nondomestic Caprinae species has not been identified. This study illustrated no clear association between glutaraldehyde coagulation testing results and nondomestic Caprinae neonatal survivability. There is evidence of inconsisten-

cy in hypogammaglobulinemia for different nondomestic species.[6,15] Thus, the lack of association may be due to species differences.

The sodium sulfite precipitation test (BOVA-S) has shown a link between FPT and inadequate serum Ig levels in domestic Caprinae.[11,17] This method allows for qualitative evaluation of primarily Ig through precipitation and turbidity. This testing method is qualitative and subjective. Traditionally, serum is added to different concentrations of sodium sulfite and allowed to precipitate.[4] Turbidity in each concentration of sodium sulfite indicates a certain amount of immunoglobulins.[4] Although the single-dilution assay is thought to be a readily utilized field test in domestic calves, no other research has been published in nondomestic Caprinae species. This study found no significant association when comparing BOVA-S and nondomestic Caprinae neonatal survivability. However, this testing modality was performed least frequently in the study ($n = 40$) and was therefore eliminated from some of the statistical analyses. Nubian ibex were the only species on which this test was performed regularly and findings were not associated with increased or decreased survival.

The results of this study challenge the validity of using common FPT domestic neonatal ruminant tests, including GGT, gluteraldehyde coagulation, and BOVA-S tests, on their own to predict the survivability of nondomestic Caprinae neonates. The analysis reveals blood glucose and fibrinogen levels in the first week of life tend to be more predictive of survival at 7, 30, and 90 d.

Although analysis found that glucose and fibrinogen levels at less than 7 d old are correlated with survival, the question still remains whether they are predictive of FPT. The positive association of glucose levels with nondomestic Caprinae neonatal survival is presumably an effect of adequate nursing, which is also likely to confer passive transfer. Given that increased levels of fibrinogen after the first week were associated with higher probabilities of infectious mortality and medical intervention, increasing fibrinogen could also be considered an indirect indicator of FPT, a condition that is more likely to result in an infectious cause of death.[4] The 50% mark of neonatal infectious mortality was correlated with fibrinogen levels at or above 600 mg/dl. Such cases were rare ($n = 4$) in this study (Fig. 2). A larger sample size of nondomestic Caprinae neonates with higher fibrinogen levels would allow this threshold to be estimated more accurately. Fibrinogen is an acute phase protein and is used as a marker of inflammation in certain ruminant species.[9] The method used to detect fibrinogen levels can be affected by increased hemolysis and lipemia. The sample quality was not always recorded in the reviewed cases. There is a possibility of sampling artifact affecting fibrinogen results.

Within the scope of this manuscript the total protein results were categorized into reference ranges to perform a descriptive analysis. The majority of subjects had "low" range (87.4%) TP levels. Only two neonates were observed to have high TP levels. This made it difficult to quantify a typical baseline effect of TP accurately. For this reason, TP was not included in the regression models in this study. Instead a descriptive comparison of rates across TP levels was provided for completeness. Follow-up analysis with larger sample sizes across TP levels is necessary to inform the relationship between total protein and neonate survival adequately. In the descriptive analysis low TP was associated with higher mortality rates (see Table 4). However, further research with larger sample sizes and better distribution across TP reference ranges is needed to understand better how these factors relate to survival and infectious mortality rates in nondomestic Caprinae. Understanding total protein in relation to survivability would be helpful, as this testing method is simple and provides results quickly. Low total protein has been associated with FPT and the need for medical intervention in domestic ruminants and nondomestic ruminants such as giraffe and kudu species.[3,10,15] Identifying criteria specific for nondomestic Caprinae species may result in more rapid testing results and understanding of neonatal survivability.

Medical intervention is utilized to aid in survival of neonates suspected to have FPT and could be a confounding factor in this study, because results of the various tests could have influenced clinicians' decisions for or against treatment. However, treatment did not ensure survival; among the factors evaluated, survivability was only associated with glucose, fibrinogen, and confirmed nursing. For individuals in this study, major medical intervention included hospitalization, plasma transfusion or euthanasia, and these animals had a lower survival rate at age 90 d compared to individuals who did not receive intervention. Similarly, infectious death rates were much higher among individuals who received intervention. This would suggest that, as expected, intervention was more often performed on less viable neonates; a neonate with declining

health has an increased likelihood of death in comparison to a neonate who does not require major medical intervention. Further research is needed to evaluate the efficacy of different medical interventions.

As expected, individuals confirmed to nurse from the dam or given colostrum supplementation prior to diagnostic testing had higher glucose levels and an increased chance of survival. Neonates who were confirmed to have nursed also had a lower likelihood of major medical intervention. The odds of major medical intervention were reduced by 50% for every 15 mg/dl of glucose found in the serum.

Larger sample sizes among subgroups, longer or more frequent follow-up periods, or incorporating longitudinal measurements of glucose and fibrinogen beyond the time of initial exam may provide better evaluation of diagnostic testing methods as predictors of survival. Other factors which have previously been identified to correlate between domestic Caprinae species and passive transfer status should be considered including weight changes.[14] Also, certain species were over- and underrepresented, which could bias the results toward Sudan Barbary sheep (*Ammotragus lervia*), Nubian ibex (*Capra nubiana*), and Cretan goats (*Capra aegagrus cretica*) in particular.

Overall, glucose and fibrinogen were found to be the best predictors of neonatal survivability, infectious disease mortality, and major medical intervention in this study. The GGT, gluteraldehyde coagulation, and BOVA-S tests, when evaluated individually, were not good predictors of neonatal survivability in nondomestic Caprinae. Further research will be required to determine if the use of multiple testing methods concurrently could better predict FPT and survival in these animals.

CONCLUSIONS

The findings suggest that the results of the GGT, glutaraldehyde coagulation test, and BOVA-S were not accurate in predicting survival of Caprinae neonates or death due to infectious disease, and thus their usefulness as sole tests of passive transfer remains unclear. Total serum protein results were not considered for statistical significance in this study. Glucose and fibrinogen were found to be the best predictors of neonatal survivability, infectious disease mortality, and the need for medical intervention. Neonates confirmed to have nursed from the dam or given a colostrum supplement were more likely to have higher glucose and less likely to receive medical intervention. Higher fibrinogen was associated with increased infectious mortality and medical intervention. Further investigation into the use of multiple concurrent testing methods in these species is warranted. The continued exploration of testing methods in the subfamilies of these species to identify specific and consistent ranges of glucose and fibrinogen for use in evaluation of failure of passive transfer and viability should be considered in future research.

Acknowledgments: The authors thank the San Diego Zoo Wildlife Alliance Collection Husbandry Science Department, and the clinical laboratory and veterinary services teams.

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Accepted for publication 20 September 2021