

Electrolyte Concentrations and Blood Gas Values in Neonatal Calves With Diarrhea

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Abstract

Portable blood analyzers, which recently have been introduced to veterinary medicine, can facilitate immediate identification of sick calves in livestock farms. However, no appropriate standard values exist for neonatal calves; therefore, reference values for adult cattle guide diagnosis and treatment of newborn calves. Our goal was to determine electrolyte, blood chemistry, and blood gas values from healthy calves and compare them to those for diarrheic calves, thus providing useful information for diagnosis and prognosis. We evaluated 193 calves (1 month old), including those with ($n = 88$) and without diarrhea ($n = 105$), using two-tailed, independent t tests after determining normality (Shapiro–Wilk test). Electrolyte measurements in the diarrheic calves included significant decreases in sodium and significant increases in potassium, chloride, and blood urea nitrogen. Strong ion difference (SID), pH, bicarbonate, partial pressure of carbon dioxide, and base excess (BE) were significantly lower in the diarrheic calves ($p < 0.001$); the anion gap (AG) was significantly higher among diarrheic calves aged 1-10 days ($p < 0.001$) compared to healthy calves. Our results demonstrate that SID, pH, bicarbonate, and BE correlated strongly with metabolic acidosis, suggesting that these indicators, including AG, can be important tools for evaluating calves' health status and for providing useful information to diagnose diarrhea.

Background

Currently, studies on calves focus primarily on epidemiological surveys of disease outbreaks. Among these outbreaks, neonatal calf diarrhea is associated with high mortality rates worldwide, resulting in severe economic losses to cattle producers due to the costs associated with medical treatment as well as to animal weakness and retarded growth [1–5]. Most diarrheic calves become ill before weaning. Many studies performed in the Republic of Korea have focused mainly on identifying pathogens associated with diarrheal illness [3, 6–8]. However, etiologies associated with diarrheal illness in calves are diverse and complex; disease may be secondary to infection, malnutrition, or environmental factors [5].

Diarrhea can lead to either the loss or the accumulation of water and major electrolytes; these findings have specific impact in newborn calves (≤ 1 month of age), as their dysregulation may ultimately be fatal [9–11]. Secretory, exudative diarrhea is associated with release of various ions in the plasma; of note, loss of HCO_3^- results in profound acid–base disturbances [12]. If this situation persists, a decrease in strong ion difference (SID) develops, notably caused by acidosis and acidemia, resulting in physical deterioration. Therefore, it is imperative to rapidly and accurately analyze the changes in SID that reflect the overall severity of the disease [13].

Moreover, to treat and manage diseased calves with maximum efficiency, biometric information that can accurately determine animal health status is needed, together with a way to diagnose any infection-causing pathogens. However, given the weight and volume of test equipment, these methods are currently underutilized in industrial (i.e., large) animal fields. In recent years, portable blood analyzers have become available; this equipment (e.g., i-STATs) can provide test results from blood samples within a few minutes. Widespread use of these devices has facilitated immediate identification of sick calves in

livestock farms [14, 15]. Thus, the objectives of this study were to analyze the changes in the SID in evaluations of electrolytes, blood chemistry, and blood gas profiles in both healthy and diarrheic calves so as to provide useful information for diagnosing sick calves, which ultimately may direct current clinical practices in the livestock industry.

Methods

Animal ethics

All animal procedures were conducted according to ethical guidelines for the use of animal samples, and were approved by the Jeonbuk National University (Institutional Animal Care and Use Committee Decision No. CBNU 2020-052). All procedures and possible consequences were explained to the managers of the surveyed farm, and written consent was obtained.

Sample collection

This study included 193 Korean beef calves (≤ 30 days old) raised in the Republic of Korea. The calves were divided into three groups by age: those 1–10 days of age ($n = 53$), 11–20 days ($n = 65$), and 21–30 days ($n = 75$; Table 3). Blood samples were collected from all animals through the jugular vein and were placed on a bottle roller and continuously agitated for at least 20 seconds to prevent formation of micro-clots. Fecal samples were collected after rectal stimulation to induce bowel movements; these samples were transported to the laboratory under refrigeration for examination. We examined the samples and subdivided them into solid, semisolid, loose, and watery; the solid and semisolid vs. loose and watery samples were classified as normal feces and as diarrhea, respectively. We also conducted a physical examination using the skin-tenting test and determining the degree of dehydration.

Table 3
Classifications and numbers of calves used in this study by age

	1–10 Days	11–20 Days	21–30 Days	Total
Healthy calves	18	39	48	105
Diarrheic calves	35	26	27	88
Total	53	65	75	193

Fecal examination

Initially, we screened fecal samples using a rapid diagnosis antigen test kit (BoviD-5 Ag) to identify antigens associated with pathogens including *Cryptosporidium parvum*, *Giardia duodenalis*, *Escherichia coli*, coronavirus, and rotavirus. These samples were also examined by reverse transcriptase–polymerase chain reaction targeting bovine viral diarrhea virus (BVDV) and *Salmonella* spp., as well as the five pathogens noted above. BVDV, coronavirus, rotavirus, *E. coli*, *Salmonella* spp., *C. parvum*, and *G. duodenalis* are major pathogens associated with diarrhea in calves [35, 36]. Diarrheic calves in this study

tested positive to one or more of the pathogens associated with diarrhea; none of these pathogens were detected in fecal samples from healthy calves. In this study, cases of diarrhea were not subdivided into bacterial, viral, and parasitic aetiologies.

Electrolyte, chemistry, and blood gas analyses

Blood parameters were measured in the field immediately after obtaining fecal samples using the EC8 + i-STAT cartridge (Abbott, Princeton, NJ, USA). Anion gap (AG) and base excess (BE) values were calculated from the concentrations of the major electrolytes Na^+ , K^+ , Cl^- , and HCO_3^- . The SID was calculated based on the combined electrolyte concentrations; $\text{SID} = ([\text{Na}^+] + [\text{K}^+]) - [\text{Cl}^-]$. Blood urea nitrogen (BUN) and glucose levels were evaluated in serum; pH, and partial pressure of CO_2 (pCO_2) were also measured.

Statistical analysis

Statistical analysis was performed using the SPSS Statistics 25 software package for Windows (SPSS Inc, Chicago, IL, USA). Results are presented as mean \pm standard error of the mean (SEM). Differences in blood test results were compared using two-tailed independent *t*-tests after documenting normality (Shapiro-Wilk test). Multiple linear regression analysis with stepwise exclusion was used to test the association between the age of calves and clinicopathological variables. In addition, the differences in the clinicopathological variables between the two groups were determined using multivariate logistic regression analysis. Odds ratio (OR) and 95% confidence intervals (CI) were calculated to determine the likelihood of diarrhea association. A *p*-value of less than 0.05 was considered statistically significant.

Results

We clinically determined the presence of diarrhea by physical examination, including the skin-tenting test, stool status, body temperature, and degree of dehydration. Also, CBC (Hct, RBC, Hb) and chemistry data (e.g., serum protein) tests were also performed to determine grouping of the healthy and diarrheic calves (data not shown). In particular, the values of Hct and serum protein in the diarrheic calves were significantly increased compared with those of the healthy calves.

Seven pathogens were detected from the 88 diarrheic calves (Table 1). Rotavirus was the most common (30/88, 34.1%), followed by *C. parvum* (5/88, 5.7%), *Eimeria* spp. (3/88, 3.4%), *G. duodenalis* (2/88, 2.3%), and BVDV (1/88, 1.1%) and coronavirus (1/88, 1.1%); no samples were found to be positive for *Salmonella* spp. In 10 fecal samples, the pathogens listed above were not detected. Diarrhea caused by viral infection was the most common. Twenty-eight (31.8%) and 8 (9.1%) calves were infected with double and triple pathogens, respectively (Table 1).

Table 1
Number of diarrheic calves infected with enteropathogens.

	Pathogens	1-10 Days (n= 35)	11-20 Days (n= 26)	21-30 Days (n= 27)	
Single	Rotavirus	12	10	8	
	Coronavirus	1	0	0	
	BVDV	0	1	0	
	<i>Cryptosporidium parvum</i>	3	0	2	
	<i>Giardia duodenalis</i>	0	1	1	
	<i>Eimeria</i> spp.	0	0	3	
Double	Rotavirus + BVDV	3	2	2	
	Rotavirus + Coronavirus	1	0	0	
	Rotavirus + <i>E. coli</i>	3	1	0	
	Rotavirus + <i>C. parvum</i>	1	3	0	
	Rotavirus + <i>Eimeria</i> spp.	0	1	3	
	BVDV + <i>E. coli</i>	1	0	0	
	Coronavirus + <i>G. duodenalis</i>	1	0	1	
	<i>C. parvum</i> + <i>G. duodenalis</i>	1	0	0	
	<i>C. parvum</i> + <i>Eimeria</i> spp.	0	1	0	
	<i>G. duodenalis</i> + <i>E. coli</i>	0	1	1	
	Triple	Rotavirus + BVDV + <i>C. parvum</i>	2	2	0
		Rotavirus + Coronavirus + <i>C. parvum</i>	0	1	0
Rotavirus + Coronavirus + <i>E. coli</i>		0	0	1	
Rotavirus + <i>E. coli</i> + <i>G. duodenalis</i>		1	0	0	
Coronavirus + <i>C. parvum</i> + <i>G. duodenalis</i>		0	1	0	
Unknown	4	1	5		
Total	35	26	27		

Sodium concentrations measured in blood samples from the diarrheic calves were significantly lower among those aged 1-10 days ($p < 0.01$) and 21-30 days ($p < 0.001$) compared to the healthy calves (Table 2). Mean potassium levels in the healthy calves gradually decreased with age, whereas the

concentrations of potassium were significantly higher among the diarrheic calves aged 1–10 days ($p < 0.01$) and 21–30 days ($p < 0.05$; Table 2). Little variation of chloride concentration was found among the healthy calves; however, in the diarrheic calves, the concentrations of chloride were significantly elevated for up to 20 days of age compared with age-matched groups of the healthy calves. According to our results, the increases in sodium (OR = 0.667; $p = 0.026$) and potassium (OR = 0.027; $p = 0.001$) lowered the likelihood of incidence of diarrhea. BUN levels were significantly higher in all age groups of the diarrheic calves when compared to the healthy calves (Table 2). According to multivariate logistic regression analysis, BUN levels were increased 1.7-fold in the diarrheic calves (95% CI: 1.30–2.24; $P = 0.000$) compared with the healthy calves. Serum glucose levels remained relatively constant among the healthy calves. By contrast, the diarrheic calves exhibited lower concentrations of glucose; however, these values increased steadily with age. Values obtained from the diarrheic calves were significantly lower than those of the healthy calves among those aged 11–20 days (Table 2).

Table 2
Results of electrolyte, BUN, and glucose testing in healthy and diarrheic calves by age.

Variables	Calf	1–10 Days	11–20 Days	21–30 Days	1 Month
Na ⁺ (mEq/L)	Healthy	142.7 ± 3.7	139.0 ± 3.2	139.6 ± 1.6	140.0 ± 3.0
	Diarrheic	137.7 ± 7.1 ^b	139.7 ± 5.6	129.2 ± 11.3 ^c	135.5 ± 9.3 ^c
K ⁺ (mEq/L)	Healthy	5.8 ± 0.5	5.3 ± 0.7	5.0 ± 0.6	5.3 ± 0.7
	Diarrheic	6.2 ± 1.6 ^b	4.6 ± 0.9	5.3 ± 1.8 ^a	5.5 ± 1.6
Cl ⁻ (mEq/L)	Healthy	99.4 ± 2.3	98.3 ± 2.2	98.9 ± 2.3	98.8 ± 2.3
	Diarrheic	105.5 ± 9.3 ^b	108.1 ± 8.8 ^c	96.6 ± 13.0	103.3 ± 11.4 ^c
AG (mEq/L)	Healthy	17.4 ± 4.6	16.7 ± 4.4	15.8 ± 2.5	16.4 ± 3.7
	Diarrheic	22.8 ± 3.9 ^a	22.1 ± 3.0	20.3 ± 4.2	21.8 ± 3.9 ^c
BUN (mg/dL)	Healthy	9.8 ± 4.9	9.0 ± 3.1	8.1 ± 2.8	8.8 ± 3.4
	Diarrheic	46.9 ± 30.7 ^c	41.6 ± 32.4 ^c	55.0 ± 34.7 ^c	48.1 ± 32.5 ^c
Glucose (mg/dL)	Healthy	104.6 ± 19.3	109.5 ± 18.7	109.0 ± 20.8	108.4 ± 19.6
	Diarrheic	83.8 ± 46.2	90.3 ± 40.2 ^b	115 ± 67.2	95.6 ± 53.6 ^a
Data are presented as mean ± SEM.					
p values were obtained using two-tailed, independent t -tests comparing results from healthy and diarrheic calves					
^(a) $p < 0.05$, ^(b) $p < 0.01$, ^(c) $p < 0.001$.					
Na ⁺ : sodium; K ⁺ : potassium; Cl ⁻ : chloride; BUN: blood urea nitrogen; AG: anion gap					

SID was significantly lower among the diarrheic calves at all ages compared with the healthy calves ($p < 0.001$); this difference was most significant in the diarrheic calves aged 21–30 days ($p = 0.0001$; Fig. 1). A decrease in SID was among the most significant contributors to the changes observed in pH and bicarbonate (HCO_3^-) concentration. The mean pH value in blood differed little among the healthy calves of all ages; however, blood pH was significantly lower among all diarrheic calves when compared to their healthy counterparts ($p < 0.001$; Fig. 1). Furthermore, HCO_3^- concentrations were also significantly lower in all age groups of the diarrheic calves compared to the healthy calves ($p < 0.001$; Fig. 1). Interestingly, the values calculated for AG decreased with age in both the healthy and diarrheic calves. The values of AG were generally high in the diarrheic calves and were significantly higher among those aged 1–10 days ($p < 0.01$; Table 2). Diarrhea was significantly associated with the increase of AG values (OR = 2.2, 95% CI: 1.36–3.56; $p = 0.001$). The mean values calculated for BE in the healthy calves varied widely, although none of the differences reached statistical significance. In contrast, BE values calculated for the diarrheic calves were significantly reduced among all age groups ($p < 0.001$; Fig. 1).

Discussion

Diarrhea is a major problem in calves less than one month of age and is of tremendous economic importance. Diarrhea results in electrolyte imbalance, dehydration, and metabolic acidosis [16–20]; however, only a few studies available have focused on acid–base balance, serum chemistries, and blood gas parameters associated with diarrhea caused by infectious agents in neonatal calves [21, 22]. Unfortunately, because the information currently available for healthy young Korean native calves is not well documented, reference values for adult cattle have commonly been used to direct therapy. In our study, we examined electrolytes, serum chemistries, and blood gas parameters in both healthy and diarrheic calves through rapid and accurate field testing. The results showed that SID, pH, bicarbonate, and BE were significantly decreased, whereas BUN and AG were significantly increased in diarrheic calves compared with healthy calves. As such, these parameters provide both critical and accurate information for treatment and prognosis.

Our findings revealed significant changes in plasma electrolyte concentrations (Na^+ , K^+ , and Cl^-) that varied according to diarrheic calf age. Our results documented an overall decrease in sodium and overall increase in potassium, chloride, and BUN concentrations in diarrheic calves when compared with healthy calves. The decrease in sodium concentration can be explained by increased intestinal loss [23]; this situation results in a concomitant decrease in plasma sodium concentration accompanied by an increase in chloride concentration.

Moreover, the significant decrease in SID values was identified in the diarrheic calves; this finding can be explained by the combination of hyponatremia and hyperchloremia [11]. The decrease in SID represents the key role played by hyponatremia in this setting, which can be attributed to excessive loss of sodium into the gastrointestinal tract as well as decreased milk intake due to anorexia; the combination of these

factors results in acidemia and strong ion acidosis [24, 25]. As such, this study highlights the role of strong ions in the acid–base status in diarrheic calves.

In addition, we detected increases in potassium concentration in diarrheic calves. Hyperkalemia has clinically been associated with acidemia and decreased intracellular pH due to electrolyte imbalance [20, 26]. While we did not include the results of packed red cell volume in these neonatal calves, we did note significant dehydration among the diarrheic calves aged 1–10 days, a finding that explains the hyperkalemia observed among diarrheic calves. Interestingly, BUN levels were significantly higher in the diarrheic calves when compared with the healthy calves, findings that are consistent with previous results [27–29]. The significant increase in BUN at all age groups was associated with a decreased glomerular filtration rate due to dehydration; this also contributed to the acidemia and metabolic acidosis observed [30]. Taken together, our results suggest that potassium and BUN can be used as appropriate measurements for evaluating the severity of diarrhea in calves.

Blood gas analysis also provides valuable information for diagnosis, prognosis, and identification of therapeutic options [31]. In this study, we observed significant alterations in acid-base homeostasis. Of particular note, bicarbonate levels were significantly lower among diarrheic calves compared to their healthy counterparts. This finding is closely associated with reductions in sodium and increases in potassium concentrations. The significant decline in bicarbonate in diarrheic calves is indicative of severe metabolic acidosis; these findings were associated with a marked decrease in blood pH as would be anticipated for acidotic calves [32]. Our results reveal a correlation between pH and animal health and suggest that blood pH may be a useful indicator of clinical status of diarrheic calves.

We found that blood gas analysis is an important indicator for determining the prognosis of and setting treatment policy for calves. In particular, calves with severe diarrhea showed a pH of less than 7.1, a HCO_3^- value of less than 20, and minus value for BE. Therefore, calves showing such decreasing values were judged as having a poor prognosis, and intensive treatment was performed, or the calf was recommended to a clinician. Mild diarrheic calves (pH 7.2 ~ 7.4) can have their acidosis corrected with a lactated ringler solution (Hartman's solution) injection. However, severe diarrheic calves (pH < 7.1) could have their acidosis corrected with intravenous bicarbonate. To prevent the occurrence of metabolic alkalosis due to excessive administration of bicarbonate, BE value was used to determine an appropriate dosage.

Likewise, values calculated for AG were higher in the diarrheic calves than in the healthy ones. Changes in AG may be attributed to variations in unidentified strong anions that include D -lactate, ketones, phosphate, and inorganic anions [25, 33]. Although we cannot draw specific conclusions because concentrations of these biological acids were not measured directly in this study, we speculate that their levels may be increased in diarrheic calves [33]. In addition, acidemia in hyperkalemic diarrheic calves was associated with a decrease of sodium and increase of AG [34].

Finally, BE values were significantly reduced in the diarrheic calves, which may contribute to the estimation of the degree of metabolic acidosis and clinical status. Of note, all calves evaluated in this study were able to stand and suck at feeding time but preferred to remain in sternal recumbency. This may explain the significant correlation among BE values, levels of dehydration, and metabolic acidosis. Consequently, on the basis of our results, we propose that calf health may be determined by blood pH, bicarbonate levels, and BE as opposed to the other parameters measured.

A limitation of our research is that we did not perform continuous follow-up studies with the diarrheic calves, and we could not exactly predict the factors associated with death in those with severe diarrhea. However, we believe it is meaningful to establish the biochemical and blood gas values of neonatal Korean native calves according to age and to compare these values with healthy and severe diarrheic calves, as we did in this study.

Conclusion

In conclusion, our findings reveal that metabolic acidosis in diarrheic calves is directly associated with profound decreases in pH, bicarbonate, and BE; these values are accompanied by hyponatremia, hyperkalemia, hyperchloremia, and increases in BUN and AG. As such, our results provide useful information for the accurate diagnosis, treatment, and management of calves with diarrhea.

Abbreviations

AG: anion gap; BE: base excess; bicarbonate: HCO_3^- ; BVDV: bovine viral diarrhea virus; BUN: blood urea nitrogen; Cl^- : chloride; *C. parvum*: *Cryptosporidium parvum*; *Eimeria* spp.: *Eimeria* species; *E. coli*; *Escherichia coli*; *G. duodenalis*: *Giardia duodenalis*; Hb: hemoglobin; Hct: hematocrit; K^+ : potassium Na^+ : sodium; RBC: red blood cell; SID: Strong ion difference

Declarations

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Authors' contributions

KSC and JPH conceived the study and designed the experiments. KSC and PJH wrote the manuscript. KMP, JHK, JYK, and SEC performed the experiments. SK and DHY analyzed the data. All authors have read and approved the final manuscript.

Availability of data and materials

All data generated or analyzed during this study are included in the article.

Ethics approval and consent to participate

All animal procedures were conducted according to ethical guidelines for the use of animal samples and were approved by the Jeonbuk National University (Institutional Animal Care and Use Committee Decision No. CBNU 2020-052).

Consent for publication

Not applicable

Competing interests

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

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Figures

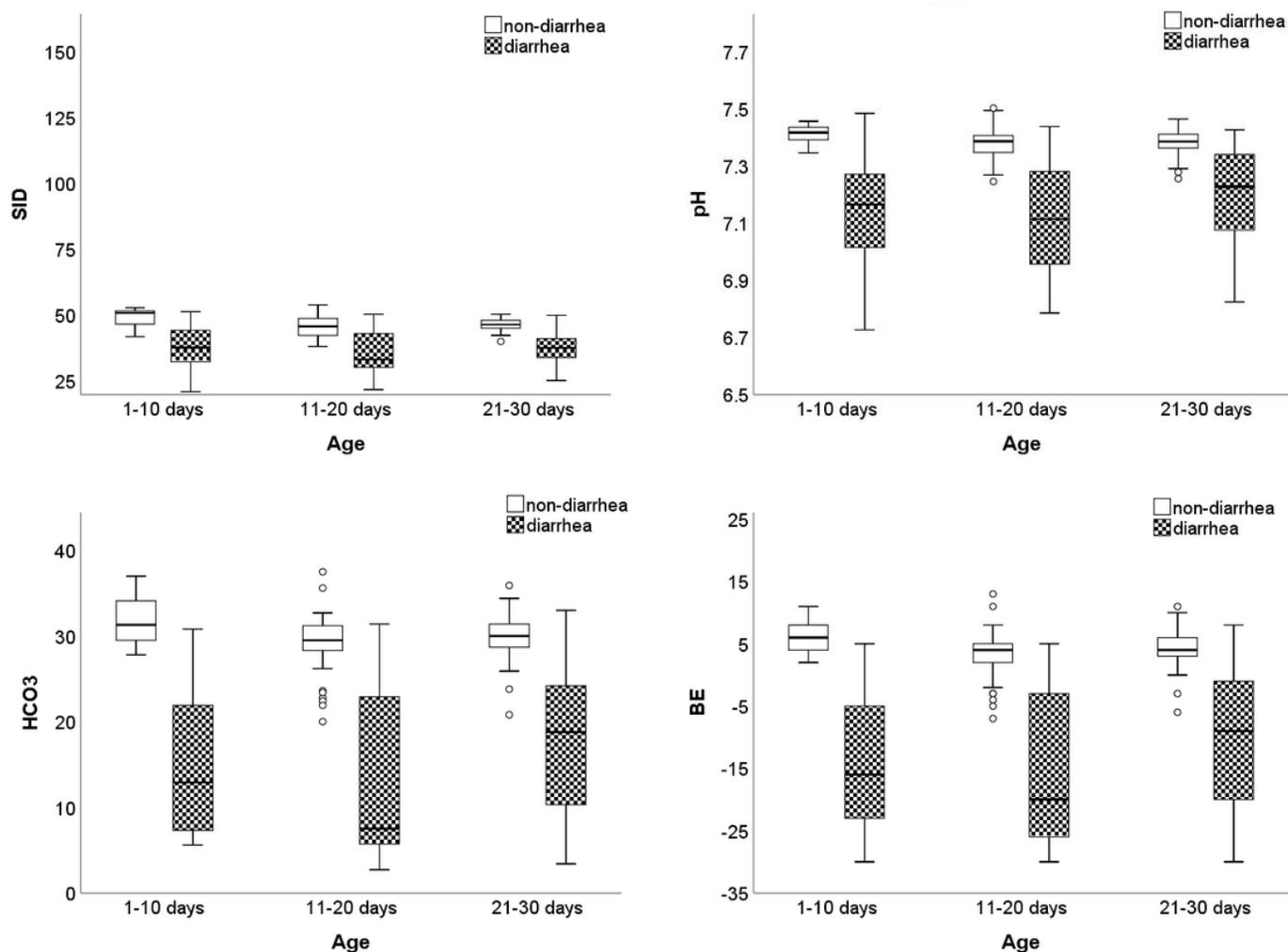


Figure 1

Box plots depicting strong ion differences (SIDs), pH, HCO_3^- , base excess (BE) in healthy and diarrheic calves by age.