HARRAN ÜNİVERSİTESİ VETERİNER FAKÜLTESİ DERGİSİ

Determination of urea, creatinine and urea/creatinine ratios in calves with diarrhoea

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Abstract: The objective of this study was to ascertain the levels of urea, creatinine (Crea) and the urea/creatinine ratio (UCR) in calves presenting with diarrhoea. The material of the study consisted of 20 calves with diarrhoea and 10 healthy calves. Once the aetiology of diarrhoeal calves had been determined, blood samples were taken, and urea, creatinine and UCR levels were determined. The findings of the study indicated that the levels of urea and UCR were statistically significantly elevated in calves with diarrhoea in comparison to the control group. However, the increase in creatinine level was statistically insignificant. The results of the study revealed that UCR is an important biomarker in the evaluation of renal failure in calves with diarrhoea.

Keywords: *Calf, creatinine, diarrhoea, urea, UCR.*

İshalli buzağılarda üre, kreatinin ve üre/kreatinin oranlarının belirlenmesi

Özet: Bu çalışmada ishalli buzağılarda üre, kreatin (Crea) ve üre/kreatinin oranının (UCR) belirlenmesi amaçlandı. Çalışmanın materyalini 20 ishalli buzağı ve 10 sağlıklı buzağı oluşturdu. İshalli buzağıların etiyolojileri belirlendikten sonra kan örnekleri alındı ve üre, kreatinin ve UCR düzeyleri belirlendi. Çalışmanın sonuçları ishalli buzağılarda kontrol grubuna göre istatistiksel olarak önemli derecede yüksek üre ve UCR düzeyi tespit edildi. Crea düzeyindeki artış ise istatistiksel olarak önemsizdi. Çalışmanın sonuçları ishalli buzağılarda böbrek yetmezliğinin değerlendirilmesinde UCR'nin önemli bir biyobelirteç olduğunu ortaya koymuştur.

Anahtar Kelimeler: *Buzağı, ishal, kreatinin, UCR.*

Introduction

Gastrointestinal disease affecting weaned calves, calf diarrhoea, is an important disease in veterinary medicine (Maier et al., 2022). The most frequently identified etiological agents in the aetiology of the disease include *Escherichia coli* (*E. coli*), *Giardia duodenalis*, coronavirus, *Cryptosporidium parvum* (*C. parvum*), and rotavirus (Balıkçı et al., 2024; Keleş et al., 2022; Mamak et al., 2023). Infectious agents are responsible for intestinal damage and a significant loss of body fluids within the intestine. This results in a rapid onset of dehydration in the calf (Kasa et al., 2020). Additionally, calf diarrhoea can result in dehydration, as well as electrolyte imbalance, metabolic acidosis, hypovolaemia and, over time, renal failure (Shehta et al., 2022).

Urea and creatinine (Crea) are commonly employed parameters in the assessment of renal failure in calf diarrhoea (Akyüz et al., 2022; Yanar et al., 2023). Nevertheless, the urea-creatinine ratio (UCR) has been a commonly employed metric in the field of human medicine in recent years (Statlender et al., 2024; Tonomura et al., 2023). The evidence suggests that UCR may serve as an effective marker for the assessment of renal failure. Furthermore, recent studies have indicated that UCR may serve as a prognostic indicator in humans (Brookes and Power 2022; van der Slikke et al., 2020). Nevertheless, the utilisation of UCR in veterinary medicine remains relatively constrained in comparison to its application in human medicine. In the literature review, there are very few studies evaluating UCR in calves with diarrhoea (Wiest and Klee, 1998).

In this context, the objective of this research was to evaluate the UCR level in calves with diarrhoea. The UCR level may serve as a suitable parameter in patients with renal failure resulting from dehydration, particularly in calves with diarrhoea, or in veterinary practice for the evaluation of direct renal failure.

Materials and Methods

Study design: The study population consisted of 20 calves (n=20) aged 1–10 days admitted to the Atatürk University Veterinary Faculty Animal Hospital large animal clinic with diarrhoea. A control group of 10 healthy calves (n=10) was also included. The study was approved by the Atatürk University Local Ethics Committee of Animal Experiments (Decision Number: 2024/18). To be eligible for inclusion in the study, calves with diarrhoea had to have received no prior treatment. Calves undergoing any form of treatment were excluded from the study. A faecal sample was initially obtained from diarrheal calves using a swab, and the aetiology of the diarrhoea was subsequently determined using a rapid test kit for five infectious agents, including *E. coli* (ETEC F5), *Giardia duodenalis*, coronavirus, *parvum* and rotavirus.

Blood sampling: Blood samples were collected from the *Vena jugularis* of calves presenting with diarrhoea and placed into serum tubes of approximately 10ml capacity. The serum samples were maintained at room temperature for 30 minutes and subsequently subjected to centrifugation at 3000 rpm for 10 minutes in a Beckman Coulter Allegra® X-30R centrifuge (USA) to obtain serum samples. Immediately following the determination of the serum samples, urea and crea measurements were performed using an auto analyser (Beckman Coulter® AU5800, USA). The urea-creatinine ratio was calculated using the following formula:

Urea/Creatinine ratio: The ratio of serum urea/serum crea was calculated.

Statistical Analysis: Before statistical analysis, the normality of the data distribution was tested using the Shapiro–Wilk test. Since the data obtained in this study did not have normal distribution, it was subjected to analysis using the Mann-Whitney *U* test, a non-parametric statistical test. Statistical analyses were performed using SPSS 27.0 software, with significance set at $P < 0.05$ to detect statistical differences between group.

Results

The results of the etiological analysis revealed that the most prevalent infectious agent was *E. coli*, with a prevalence rate of 60% (12/20). Furthermore, three calves exhibited signs of rotavirus-induced diarrhoea (3/20), while five calves displayed a rotavirus, coronavirus and *C. parvum* mixed infection (5/20).

The results of the biochemical analyses indicated a statistically significant ($P < 0.001$) elevation in urea levels (130.93 mg/dL [69.99-245.23 mg/dL]) in the calves with diarrhoea compared to the control group (29.02 mg/dL [0.98-45.20 mg/dL]) (Table 1). Furthermore, the concentration of crea in the serum of calves with diarrhoea (2.51 mg/dL [1.44-4.07 mg/dL]) was observed to be higher than that of the control group (2.3 mg/dL [0.09-2.97 mg/dL]). However, this elevation was not found to be statistically significant. Finally, the UCR was found to be significantly elevated ($P < .001$) in the diarrhoeic group (53.70 [31.88-125.12]) in comparison to the control group (14.22 [9.15-22.94]).

Discussion and Conclusion

The objective of this study was to ascertain the UCR level in the assessment of renal damage in calves with diarrhoea. In the study, *E. coli* was the most frequently identified agent in calves with diarrhoea. This finding is not aligned with the results of prevalence studies investigating the aetiological causes of calf diarrhoea in various provinces of Turkey (Balıkçı et al., 2023; Mamak et al., 2023). It is, however, no prevalence study was conducted in the region where the study was conducted. Moreover, it has been established that *E. coli*-induced calf diarrhoea represents a significant global health concern (Coşkun and Şahin 2023; Nguyen et al., 2011). In light of these findings, it is possible that the prevalence of calf diarrhoea in the Erzurum region may differ from the levels reported in the literature.

In the study, the serum urea level was found to be statistically significantly higher (P<.001) in calves with diarrhoea compared to the control group. These results were in line with previous reports (Eğlenti et al., 2020; Saleh et al., 2022). It is important to note, however, that there is also a study reporting non-statistically significant increases in urea levels due to diarrhoea (Torche et al., 2020). The discrepancies in clinical severity observed in the calves included in this study may be the underlying cause of these contradictory results. Dehydration and hypovolemia resulting from diarrhoea in calves (Kozat, 2021; Shehta et al., 2022) may lead to pre-renal azotemia (Molitoris, 2022), which could explain the observed increase in urea levels. Furthermore, the elevation in urine concentration resulting from dehydration may also be a contributing factor to the observed increase in urea levels (Thomas et al., 2008) as urea is an important factor in increasing urine concentration (Yang et al., 2005). In addition, previous studies have indicated that gastrointestinal bleeding may also be a contributing factor to elevated urea levels (Stellato et al., 1980; Tomizawa et al., 2015). In this study, the *E. coli* infection agent was detected in the majority of calves presenting with diarrhoea (60%), and no clinical signs indicative of gastrointestinal haemorrhage were observed in the calves. In light of these findings, it is reasonable to suggest that the elevated urea levels observed in calves with diarrhoea are due to dehydration and hypovolemia rather than gastrointestinal haemorrhage.

Table 1. Urea, crea and UCR levels of healthy and diarrhoeic calves.

Parameters	Control Medians (Range)	Diarrhoea Medians (Range)	*P* Value
Urea (mg/dL)	29.02 (0.98-45.20)[a]	130.93 (69.99-245.23)[b]	*P*<.001
Crea (mg/dL)	2.3 (0.09- 2.97)	2.51 (1.44-4.07)	*P*=0.448
UCR	14.22 (9.15-22.94)[a]	53.70 (31.88-125.12)[b]	*P*<.001

a, b The means shown in different lowercase letters between the groups (on the line) are statistically significant.

The crea values of the diarrhoeal calves were observed to be higher than those of the control group; however, this increase was not found to be statistically significant. This result was not consistent with previous reports (Akyüz and Kükürt, 2021; Makdam and Basbugan, 2020). This result of the study may be due to insufficient protein intake of the calves. Studies have shown that crea levels may increase when protein intake is insufficient (Valtonen et al., 1982). In this context, a partial increase in crea levels in calves may have occurred due to insufficient protein intake. Strikingly, however, the result of a recent study shows that there may be statistically significant or insignificant increases in crea levels depending on the etiological factors of calf diarrhoea. Furthermore, in this study, the increase in crea levels in calves infected with *E. coli* was statistically significant compared to the control group, whereas the increase in calves infected with rotavirus was not statistically significant (Tümer and Dincer, 2024). Although the majority of pathogens detected in calf diarrhoea in this study were *E.coli*, it is important to report the presence of calves with rotavirus infection. In this context, it can be argued that the CRE level in calf diarrhoea may vary depending on the aetiological agent.

The UCR level was found to be statistically significantly higher in the diarrheal group than in the control group. This finding was consistent with the results of previous human studies, which have demonstrated that UCR can be used as a prognostic marker in patients with renal failure (Brookes and Power, 2022; Tonomura et al., 2023). In the literature review, the number of studies on this subject in the field of veterinary medicine is relatively few (Wiest and Klee, 1998; Lobetti, 2012). However, the reason for the increased UCR level in human studies remains unclear. At this juncture, the potential mechanism may be attributed to a multitude of effects exerted by urea, including disruption of the intestinal epithelial barrier and alteration of the microbiome (Lau and Vaziri, 2017; Seki et al., 2019). In calves with diarrhoea, the impairment of the epithelial barrier and flora may have triggered a relative increase in urea level compared to creatinine level, leading to a statistical increase in UCR level. Nevertheless, further research is required to ascertain the impact of urea on calves with intestinal damage and to determine whether intestinal damage is a contributing factor to the elevation of serum urea levels in these patients. However, within the context of this study, it was established that UCR levels can be employed in the assessment of renal failure in calves with diarrhoea.

In conclusion, this study has demonstrated that UCR level, which has been frequently used in the evaluation of renal failure in human medicine in recent years, may act as an important marker for the evaluation of renal failure in calves with diarrhoea. Furthermore, it may be useful to evaluate UCR levels in patients who may cause secondary renal failure, especially in the field of veterinary medicine.

Conflict of Interest

The authors stated that they did not have a potential or perceived conflict of interest.

Ethical Approval

The study was approved by the Atatürk University Local Ethics Committee of Animal Experiments (Decision Number: 2024/18).

Similarity Rate

We declare that the similarity rate of the article is 15% as stated in the report uploaded to the system.

Author Contributions

Design: KEY
Control/Supervision: KEY, MSA
Data Collection and/or Processing: KEY, AÖ
Analysis and / or Interpretation: KEY, AÖ
Literature Review: KEY
Writing the Article: KEY
Critical Review: MSA

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