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## Original Research

## Equine Coronavirus-Associated Colitis in Horses: A Retrospective Study

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## ABSTRACT

Equine coronavirus (ECoV) is a known cause of fever, anorexia, and lethargy in adult horses. Although there are multiple reports of ECoV outbreaks, less is known about the clinical presentation of individual horses during a nonoutbreak situation. The purpose of this study was to describe the clinical presentation of horses diagnosed with ECoV infection that were not associated with an outbreak. Medical records of all horses admitted to Washington State University, Veterinary Teaching Hospital, during an 8-year period were reviewed (2010–2018). The five horses included in this study were older than 1 year of age, were diagnosed with colitis, tested positive for ECoV using real-time polymerase chain reaction, and were negative to other enteric pathogens. Interestingly, 4 of 5 horses had moderate to severe diarrhea, 3 had abnormal large colon ultrasonography, 2 had transient ventricular tachycardia and 2 had clinicopathologic evidence of liver dysfunction. ECoV should be included as a differential diagnosis for individual horses presenting with anorexia, fever, lethargy, and colitis. Early identification of ECoV cases is key to implement appropriate biosecurity measures to prevent the potential spread of this disease.

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## 1. Introduction

Equine coronavirus (ECoV), an enveloped ribonucleic acid virus member of the Coronaviridae family, causes self-limiting infection in adult horses associated with nonspecific clinical signs, including anorexia, lethargy, and fever [1,2]. Colic, leukopenia, and changes of fecal character have also been reported [3–5]. Although the clinical signs of horses affected by ECoV during outbreaks has been reported in detail [1–5], less is known about the clinical manifestation of this infection in adult horses in nonoutbreak situations [4,6]. Thus, the purpose of this study is to describe the clinical presentation of horses diagnosed with ECoV that were admitted to a tertiary hospital, but were not associated with a known outbreak.

## 2. Materials and Methods

The medical records of all horses that were presented to the Washington State University–Veterinary Teaching Hospital (WSU-VTH) from 2010 to 2018 were retrospectively reviewed for this descriptive study. Horses were included in the study if they were older than 1 year, had clinical signs consistent with colitis, tested positive for ECoV using real-time polymerase chain reaction (RT-PCR), and tested negative for other common enteric pathogens.

Individual data collected included admission signalment, presenting complaint as defined by the owner, referring veterinarian or both, clinical signs, and blood work. Season was allocated based on the month at presentation: winter (December–February), spring (March–May), summer (June–August), and fall (September–November). Clinical signs recorded included heart rate, respiratory rate, rectal temperature, and fecal consistency (normal, soft, and diarrhea). Hematological (white blood cells count, band and mature neutrophils, lymphocytes, monocytes, eosinophils, basophils, red blood cells count, hemoglobin, packed cell volume, fibrinogen, mean corpuscular volume, mean corpuscular hemoglobin concentration, red blood distribution width, and platelets) and biochemical parameters (lactate, gamma-glutamyl transferase, aspartate transaminase, alkaline phosphatase, creatine kinase, blood urea nitrogen, creatinine, glucose, total protein, albumin,

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globulin, calcium, phosphorus, total bilirubin, sodium, potassium, chloride, carbon dioxide, and anion gap) for each case were also recorded. Lactate measurements were performed using a stall side analyzer (Lactate Plus Nova; Medical Innovation House, Runcorn, Cheshire, UK). All blood work was performed on site (Clinical Pathology Laboratory, WSU-VTH) at or within 24 hours of patient admission, and all blood smears were reviewed by a board-certified clinical pathologist. Transabdominal ultrasound (MyLabAlpha; Esaote, Indianapolis, IN) findings, treatments administered, secondary complications, days of hospitalization, final diagnostics and outcome were also included.

Fecal samples were shipped refrigerated immediately after collection, to the RT-PCR Research and Diagnostic Core facilities, at the University of California (Davis, CA), for RT-PCR panel testing, that included Equine Coronavirus, *Clostridium difficile* (*C. difficile*, genes encoding toxin A and B), *Lawsonia intracellularis*, *Neorickettsia risticii*, and *Salmonella* spp. Bacterial culture (*Salmonella* spp, *C. difficile*, and *Clostridium perfringens*) and enzyme-linked immunosorbent assay (ELISA) (*C. difficile* TOX A/B II; Techlab, Blacksburg, VA) - on fecal samples were performed at the Washington Animal Disease Diagnostic Laboratory (Pullman, WA).

A case was classified as ECoV positive if at least one fecal RT-PCR was positive for ECoV and the other enteric pathogens tested were excluded. An outbreak, for the purpose of this study, was defined as two or more horses clinically affected by ECoV on the same premises.

### 3. Results

A total of five horses met the inclusion criteria. All cases were positive for ECoV using fecal RT-PCR and were negative for the other enteric pathogens tested. The median age was nine years (range 8–13 years); all horses were geldings. Breeds included 2 Quarter Horses, 1 Arabian, 1 Tennessee Walking Horse, and 1 Miniature Horse. Three horses were used for pleasure riding; the use of the remaining two was not recorded. There was no history of recent travel for 4 horses; travel was not recorded for the fifth horse. Two cases presented in the spring, two during winter, and

one in the summer. Based on history, none of these cases were associated with other confirmed cases of ECoV.

The presenting complaints on admission were similar among all cases and included anorexia (5/5), fever (5/5), diarrhea (high volume and frequency of watery feces; 4/5) and lethargy (3/5). Colic (2/5) and soft feces (1/5) were also noted. Physical examination parameters and abnormalities observed on blood work, at or within 24 hours of admission (Table 1). Transabdominal ultrasonography was performed in all horses at admission: two horses had increased colonic wall thickness (colonic wall measurement >0.5 cm) and one had a fluid-filled large colon.

Commonly used treatments included flunixin meglumine (4/5; 0.5–1.1 mg/kg every 12 or 24 hours, intravenously), di-tri-octahedral smectite (3/5; 0.5–1.8 g/kg every 8, 12, or 24 hours, orally) (Biosponge; Platinum Performance, Buellton, CA), fluid therapy (3/5; 50–100 mL/kg every 24 hours intravenously or orally) and sulfamethoxazole/trimethoprim (3/5; 30 mg/kg every 12 hours orally). Other treatments used more sporadically include: metronidazole (1/5; 15 mg/kg every 8 hours orally or *per rectum*), calcium gluconate 23% (1/5; 15–25 mL/L of fluids intravenously), dextrose 50% (1/5; 50–100 mL/L of fluids intravenously), magnesium sulfate 50% (1/5; 1–2 mL/L of fluids intravenously), potassium chloride (1/5; 20–40 mEq/L of fluids intravenously), gentamicin (1/5; 6.6 mg/kg every 24 hours intravenously), potassium penicillin (1/5; 22,000 IU/kg every 6 hours intravenously), omeprazole (1/5; 4 mg/kg every 24 hours orally) (Gastrogard; Merial LLC, Gainesville, GA) and sucralfate (1/5; 20 mg/kg every 6 or 8 hours orally).

Secondary complications included transient ventricular tachycardia (2), hepatic lipidosis (1), and hepatobiliary dysfunction (1). Hepatic lipidosis was diagnosed on a Miniature Horse gelding based on increased liver enzymes (SDH 46 U/L, normal range 4–17 U/L; GGT 92 U/L, normal range 14–40 U/L; ALP 722 U/L, normal range 75–245 U/L), increased bile acids (17  $\mu$ mol/L, normal range 0–10  $\mu$ mol/L) and increased triglycerides (198 mg/dL, normal range 8–51 mg/dL) during hospitalization. Plasma ammonia in this case remained normal (14  $\mu$ mol/L, normal range 1–50  $\mu$ mol/L). Hepatobiliary dysfunction was diagnosed in an Arabian gelding based on increased liver enzymes (GGT 202 U/L, ALP 697 U/L, and SDH 34) and bile acids (15  $\mu$ mol/L) during hospitalization. Patients

**Table 1**

Physical examination parameters and blood work abnormalities (median (range)) observed in all ECoV-positive cases at or within 24 hours of admission.

Parameter evaluated	Median (range)	Horses with Abnormal Parameters		Reference Range
		Below (%)	Above (%)	
<b>Physical exam</b>				
Heart rate (bpm)	52 (36–70)	0	80	<40
Respiratory rate (bpm)	20 (10–42)	0	80	8–16
Rectal temperature (°C)	38.1 (37.4–38.7)	20	20	37.5–38.5
<b>Blood work</b>				
White blood cells ( $\times 10^3/\mu$ L)	5.0 (2.0–11.3)	60	20	5.5–10.5
Bands ( $\times 10^3/\mu$ L)	0.180 (0–0.812)	0	60	0–0.1
Neutrophils ( $\times 10^3/\mu$ L)	1.950 (0.580–9.040)	80	20	3.0–7.0
Lymphocytes ( $\times 10^3/\mu$ L)	1.450 (1.200–1.921)	60	0	1.5–4.0
Packed cell volume (%)	36 (31–52)	0	20	30–45
Fibrinogen (mg/dL)	500 (400–600)	0	60	100–400
Lactate (mmol/L)	2.1 (0.9–2.1)	0	40	0–2.0
Gamma-glutamyl transferase (U/L)	23 (19–25)	0	0	14–40
Aspartate transaminase (U/L)	260 (249–392)	0	0	170–435
Alkaline phosphatase (U/L)	314 (128–903)	0	60	58–228
Creatine kinase (U/L)	214 (133–871)	0	40	30–357
Creatinine (mg/dL)	1.5 (1–2.2)	0	20	0.8–1.9
Total Protein (g/dL)	6.3 (4.6–7.4)	20	0	5.6–7.5
Albumin (g/dL)	3.5 (2.8–3.7)	0	0	2.8–4.1
Globulin (g/dL)	2.9 (1.7–3.8)	20	0	1.8–4.1
Bilirubin (mg/dL)	4.6 (3.3–8.8)	0	100	0.6–2.9
Sodium (mEq/L)	135 (126–140)	20	0	132–141
Chloride (mEq/L)	100 (91–104)	40	0	96–106

were hospitalized for a median of five days (range 4–18 days) and all survived to discharge.

#### 4. Discussion

Although the clinical signs and outcomes of horses infected ECoV during outbreaks have been reported in detail [1–3], less is known about the clinical presentation of horses that are infected during a nonoutbreak situation [4]. This study describes the clinical presentation of horses that presented with clinical ECoV infection to a tertiary care facility, but were not associated with a known ECoV outbreak. This retrospective study only dates back to 2010 as this was the time when ECoV testing was included in routine fecal panels in laboratories around the country [3,7].

All the cases included in this study were diagnosed with ECoV after their feces tested positive using RT-PCR as this test has shown good sensitivity and specificity [8,9]. In addition, other common enteric pathogens, including *Salmonella* spp, *C. perfringens*, and *C. difficile*, as well as *C. difficile* toxins A and B, were ruled out in all cases.

Similarly to that reported by others [1,2,4,10,11–13], the positive horses in our study were of middle age. The breeds of the affected horses reflect those breeds seen at the WSU-VTH [14]. While most reports for this infection occur during winter [3], 3 of 5 horses in our study were admitted during the spring-summer. This is not surprising and reflects the sporadic nature of this infection [14].

The most common clinical signs observed in our study included anorexia, lethargy, and fever, all characteristic of this infection [2,3]. Changes in manure consistency (diarrhea and soft feces) were observed in all of the positive horses; interestingly, this is higher than previously reported [2–4,6]. Factors such as the duration of clinical signs and previous treatments administered before admission, variations of viral load and virulence of virus strain, and regional differences may explain the high number of cases presenting watery feces. A previous study at our institution showed an overall incidence of colitis of 12.3%. For the majority of these cases, an infectious agent was not identified [14].

The clinicopathological and transabdominal ultrasound findings were supportive of a diagnosis of colitis in all the horses included in our study. Abnormal ultrasound of the large colon has been previously reported with this infection [4]. Abnormalities of clinical relevance at admission included tachycardia, tachypnea, and hyperlactatemia likely the result of hemoconcentration and/or endotoxemia [2–4,7,13,15]. These changes, associated with the observed leukopenia, characterized by left shift, neutropenia and lymphopenia as well as hyperfibrinogenemia, are consistent with an acute inflammatory disease process and are commonly seen with colitis and have been previously reported in ECoV cases [2–4,7,8]. The increase in total serum bilirubin observed in our cases is likely the result of anorexia [16,17].

The hepatic lipidosis observed in the Miniature Horse is likely associated with anorexia [10,18]. Liver dysfunction and failure have been reported in ECoV before and may result from endotoxemia and/or bacteremia secondary to gastrointestinal translocation [2,4,7].

The ventricular tachycardias observed in our cases were transient and not unexpected. Arrhythmias occurring secondary to gastrointestinal disease are encountered more frequently in horses than rhythm disturbances associated with primary myocardial

pathology [17]. Ventricular arrhythmias are not uncommon in cases of endotoxemia, colitis, and other systemic diseases that may cause electrolyte or metabolic disturbances [16,19]. The constant clinical monitoring provided at tertiary facilities such as our institution may have increased the chances of arrhythmia diagnosis in these cases. Consistent with previous reports [2–4,7], all horses had a positive response to supportive treatment and were hospitalized for a short period.

Considering that ECoV is not shed routinely in the feces of horses [14], and that other common infectious causes of enterocolitis were ruled out in all of these cases, it is likely that the colitides observed in the horses included in our study were caused by ECoV.

Although our cases were not associated with known outbreaks, ECoV should be included as a differential diagnosis for horses presenting with anorexia, fever, lethargy, and colitis, until more is known, as this organism is shed for 2–5 weeks in feces of affected horses and has been shown to cause outbreaks [2,7,9,13,20]. Thus, early identification of ECoV cases is key to implement appropriate biosecurity measures to prevent potential transmission of this disease.

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