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Endoscopic and Histopathological Assessment in Chronic Inflammatory Enteropathy of dogs

Abinaya Santhamoorthy[1], Kavitha Santhakumar[1*], Selvaraj Palanisamy[1], Pazhanivel Natesan[2], Pothiappan Ponnusamy[1] and Parthiban Sivamurthy[3]

[1]Department of Veterinary Clinical Medicine– Tamil Nadu Veterinary and Animal Sciences University, Chennai, INDIA
[2]Department of Veterinary Pathology – Tamil Nadu Veterinary and Animal Sciences University, Chennai, INDIA
[3]Department of Animal Biotechnology- Tamil Nadu Veterinary and Animal Sciences University, Chennai, INDIA

** Corresponding author: S. Kavitha: E-mail: kavikrithigaa@gmail.com*

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ABSTRACT

Diseases of the intestines are many a times hidden challenges. One such challenge is Chronic inflammatory enteropathy (CIE) is characterised by the presence of persistent or recurrent gastrointestinal signs includes diarrhoea, vomiting and weight loss for more than three weeks. CIE dogs were categorised into food responsive enteropathy (FRE), antibiotic responsive enteropathy (ARE), steroid responsive enteropathy (SRE) and non- responsive enteropathy (NRE) based on the response to elimination trail, antibiotic treatment and immunosuppressive therapy. The study was conducted to document the canine chronic inflammatory enteropathy index, endoscopic and histopathologic changes CIE dogs. 40 dogs with chronic GI signs were selected for this study and subjected for detailed physical examination, haematology, serum biochemistry, radiography and ultrasonographic examination CIE was diagnosed in 13 dogs based on the endoscopic and histopathologic changes. Moderate form of CCECAI score was recorded highly in this study. Haematological findings of CIE dogs include leucocytosis with neutrophilia and monocytosis and no significant difference were noticed in the biochemical parameters of CIE. Increased friability and hyperaemia was the predominant endoscopic changes of CIE dogs. In all the dogs with CIE of various categories showed lymphoplasmacytic infiltration on histopathology.

HIGHLIGHTS

- CIE diagnosis was done based on the histopathological changes of endoscopic guided biopsy.
- Lymphoplasmacytic infiltration found to be major histopathological changes in all the categories of CIE.

Keywords: CIE, CCECAI, Endoscopy, lymphoplasmacytic infiltration, hyperaemia

Chronic inflammatory enteropathy is characterised by the presence of recurrent or persistent gastrointestinal signs such as vomiting, diarrhoea and weight loss for more than three weeks (Jergens *et al*., 2003; Dandrieux 2016). Routine laboratory examination, ultrasonography and radiography will serve as a supplementary tool in case of gastrointestinal disorders. Gastrointestinal endoscopy was an important diagnostic tool in the diagnosis of CIE in dogs and endoscopy provides direct and immediate visualisation/ assessment of GI tract. Finally, histopathology of the endoscopy guided biopsy will provide the definitive diagnosis (Garcıa-Sancho *et al*., 2007; Cerquetella *et al*., 2010). Chronic inflammatory enteropathy (CIE) in dogs is a complex and challenging condition that affects the gastrointestinal tract. CIE is characterized by long-term inflammation and disruption of the normal functioning of the intestinal system. This condition can lead to a wide range of clinical signs and discomfort for affected dogs.

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Understanding the causes, symptoms, and management of CIE is essential for veterinarians and pet owners to provide the best possible care for dogs suffering from this condition. Hence the current study will discuss about the CCECAI, endoscopic and histopathologic changes in different categories of CIE dogs.

MATERIALS AND METHODS

The study was conducted in the small animal medicine unit of Madras Veterinary College Teaching Hospital of Tamil Nadu Veterinary and Animal Sciences University, Chennai. Dogs (n=40) presented with chronic GI signs were selected for the study and subjected for detailed physical examination, haematology, serum biochemistry, diagnostic imaging, Endoscopy and histopathological examination. Other possible causes of chronic GI signs recorded such as exocrine pancreatic insufficiency, parasitic worm infestation, foreign body, mesenteric lymphoma, oesophageal nodules were excluded from this study. Haematology and serum biochemistry were performed using auto analyser. Ultrasonographic (AEROSCAN) and radiographic examination was performed as per standard procedure to exclude other causes of GI signs. Apparently healthy dogs brought for general checkup formed the control group in this study.

Canine chronic enteropathy clinical activity index (CCECAI)

The clinical activity of affected dogs was recorded using CCECAI score given by Allenspach *et al*. (2007). Based on the CCECAI score the dogs were classified into insignificant disease (0–3), mild disease (4–5), moderate disease (6–8), severe disease (9–11), very severe disease ≥12.

GI Endoscopy and Endoscopic biopsy

Preparation and restraining of the animals were done as suggested by Zoran (2001) to improve the visualization of the GI mucosa and to reduce the risk of aspiration, food was withheld for 24-48 hours, and water was withheld for 4 hours prior to the procedure. Oral laxative medication was given a day before and an electrolyte-based enema was given before for colonoscopic procedure. Endoscopic images were captured digitally. The endoscopic examination was performed as per the standard procedure described by Guilford (2005) and Richter (2005) by using a Karl Storz type No. 60714 PKS (Germany) Veterinary Video endoscope with an outer diameter of 7.8 mm, a biopsy channel diameter of 2.8 mm, and a working length of 1400 mm. A fenestrated type, long oval cup biopsy forceps (Karl Storz) of 2.2 mm diameter was used for taking a biopsy. Lesions observed during endoscopy were recorded and scored using WSAVA gastrointestinal standardization group (Washabua *et al*., 2010) and four to five representative biopsy samples were taken by using pinch biopsy forceps (Jergens and Moore, 2010).

Histopathology

Samples obtaining during endoscopy were fixed in 10% formalin and processed after three days. The biopsy samples were stained with Haematoxylin and eosin stain and the interpretation of histopathologic changes were done using WSAVA gastrointestinal standardisation group (Day *et al*., 2008; Washabau *et al*., 2010). The score was given based on the severity 0- normal, 1-mild, 2-moderate, 3- severe.

RESULTS AND DISCUSSION

GI endoscopy was performed in 20 dogs presented with chronic GI signs based on their owner consent. Based on the endoscopic examination, seven cases were excluded due to the presence of oesophageal nodules (n=4) and foreign body (n=3). CIE was diagnosed in 13 dogs based on the histopathologic changes. All these dogs were negative for parasitic ova in the faecal examination.

Breeds included were non – descript (n=4), followed by German Shepherd (n=3) and Spitz (n=2). The other breed affected include Golden Retriever, Doberman, Rajapalayam, Chippiparai with one case each. Highest incidence was noticed in non-descript dogs. Among the affected male animals showed high occurrence than the female animals. In our study high incidence was seen in non- descript breeds because of over-representation in the population. Middle aged animals were highly affected in this study. The median age of the CIE affected animals was five.

The most common clinical signs observed in CIE dogs was diarrhoea in 69.23 per cent case (9/23) characterized by

melena and haematochezia in two dogs with 15.38 per cent in each. Watery diarrhoea without blood noticed in 38.46 per cent (5/13). Mixed signs of vomiting and diarrhoea was noticed in 23.07 per cent dogs (3/13), vomiting alone in one case. Non- GI signs like pedal edema (1/13) and skin lesions (2/13) were also noticed in this study (Fig. 1). Heilman *et al*. (2014), Volkman *et al*. (2017) and Mehain *et al*. (2019) reported chronic diarrhoea and weight loss were the most commonly observed clinical signs in dogs affected with CIE.

In the present study, Highest number of cases showed CCECAI score of in moderate type (n=7) followed by severe (n=4) in CIE dogs. Mild and very severe form were recorded in one case respectively. The median score of CCECAI is eight in dogs with CIE (range 4-10). The similar findings were recorded by Procoli *et al*. (2013), Heilman *et al*. (2014), Volkman *et al*. (2017) and Linta *et al*. (2021). Their study also revealed high incidence of moderate form in CIE dogs. Waxing and waning nature of clinical signs and poor recognition of digestive complaint by the owners might be the reason for dogs present in moderate to severe form of CIE.

Faecal score of five were observed in five cases in which the consistency of faces was watery in nature. Score of 4.5 was seen in four cases wherein the faeces was liquid in nature with slight consistency. Three dogs had faecal score of four in which the faeces were poor in consistency with viscous and all form is lost. The only one dog had a score of 2. Westermarck *et al*. (2005) documented the most of the dogs affected with CIE had a faecal score of 4 and 4.5 in their study.

Haematological findings of CIE dogs were leucocytosis with neutrophilia and monocytosis. Though the significant difference noticed in the haemoglobin value of CIE dogs when compared to healthy group, the value remains within the normal range. There was no significant difference noticed in the biochemical parameters of CIE dogs (Table 1). On radiography, no changes were observed in the CIE dogs however, two dogs showed gas filled intestinal loops in lateral view.

Ultrasonography of CIE dogs revealed, intestinal wall measurements were within normal range except in three cases increased intestinal thickening were recorded. All the animals showed normal echogenicity with distinct intestinal wall layers. Ultrasonography serves as an important diagnostic tool for the GI tract of small animals presented with chronic vomiting and diarrhoea. In case of humans, intestinal thickening on the sonography was found to be associated with inflammatory bowel disease. In contrast, intestinal thickness is an insensitive and non-specific indicator of the presence and differentiation of inflammatory bowel disorders in dogs as suggested by Gaschen *et al*. (2008).

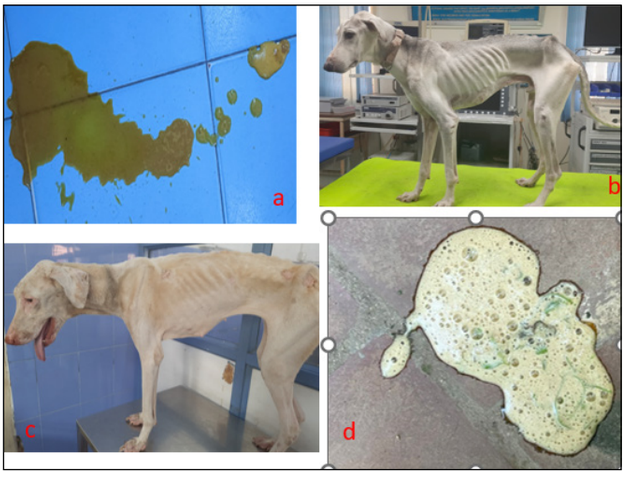

Fig. 1: Clinical signs of CIE

(a) Watery diarrhoea **(b)** emaciation of CIE dog **(c)** dog with skin lesion **(d)** vomiting

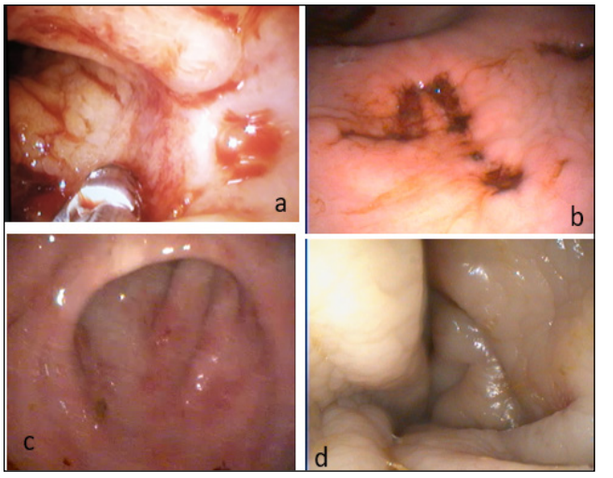

Fig. 2: Endoscopic findings of Stomach

(a) severe ulceration and friable gastric mucosa **(b)** linear ulcer **(c)** mild erosion **(d)** discolouration of the gastric mucosa

Table 1: Haematological parameters of healthy and CIE dogs

Parameters	Group I Healthy (n=10)	Group II CIE (n=13)	t value
Haemoglobin (g/dl)	15.33 ± 0.53	12.65 ± 0.83	2.54*
PCV (per cent)	40.44 ± 0.84	35.10 ± 2.21	2.02NS
RBC(×10^6/cumm)	6.39 ± 0.13	5.83 ± 0.35	1.32NS
WBC /cmm)	11020 ± 667	17107 ± 1603	3.16**
Platelet /cmm	286320 ± 30053	331784 ± 48560	0.74NS
Neutrophil /cmm	7922 ± 504.6	13169.5 ± 1256.9	3.48**
Lymphocytes /cmm	2464.4 ±169.9	3042.23 ± 345	1.37NS
Monocytes /cmm	496.8 ± 35.41	795.6 ±79	3.12**
Eosinophils /cmm	106.86 ± 8.43	139.14 ± 17.55	1.65NS

** - Statistically highly significant (P < 0.01); * - Statistically significant (P < 0.05); NS-Statistically non-significant (P>0.05); PCV- Packed cell volume, RBC- Red blood corpuscles, WBC- White blood corpuscles.

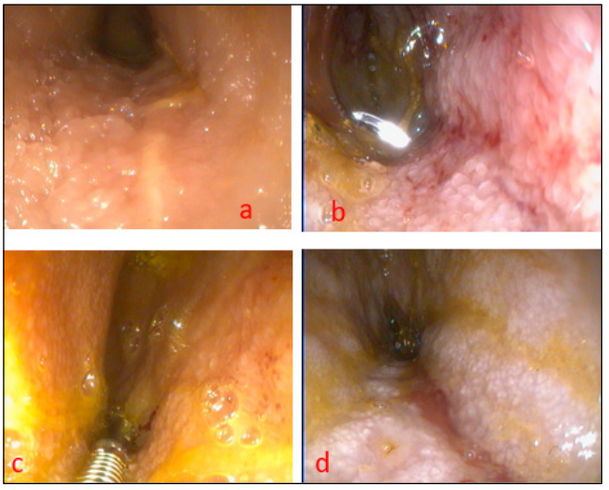

Fig. 3: Endoscopic findings of duodenum

(a) Excess mucus production in the duodenum; **(b)** erosions of duodenal mucosa **(c)** Thickened pyloric opening with bile mixed contents; **(d)** Highly fragile mucosa with corrugated appearance in the duodenum

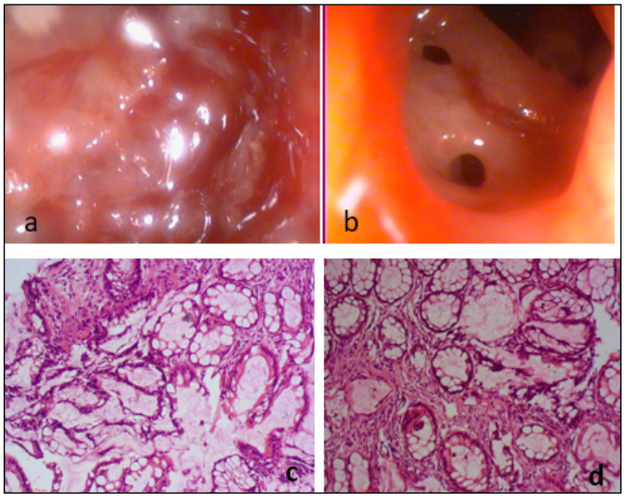

Fig. 4: Endoscopic and histopathologic findings of colon

(a) Highly friable colonic mucosa with severe ulceration **(b)** thickened and reduced lumen size with severe bleeding in the colonic mucosa **(c)** goblet cell hyperplasia with MNC infiltration **(d)** lymphoplasmacytic infiltration. c & d- haematoxylin and eosin stain (20x)

The most common endoscopic findings of the stomach were moderate friability to hyperaemia and erosion whereas in duodenum texture changes like increased granulation, corrugation and the friability were predominant changes. Increased friability and hyperaemia were the major changes in dogs presented with colitis signs (Fig. 2, 3, 4 a&b). Gastroduodenoscopy or colonoscopy in combination with endoscopically guided biopsy is regarded as one of the most useful techniques used in diagnosing chronic inflammatory diseases of the gastrointestinal tract in dogs and cats (Jergens and Simpson 2012). Garcia- Sancho *et al*. (2007) in their study recorded similar findings of hyperaemia and friability in the gastric and colonic mucosa. While Slovak *et al*. (2014) examined the entire GI tract and revealed the endoscopic changes such as erythema, friability, increased granularity/ cobblestone appearance, discolouration and ulceration/ erosion in IBD dogs. Moser *et al*. (2018) and Perez- Merino *et al*. (2022) documented increased granularity and friability as the most common endoscopic findings in the duodenal mucosa of CIE dogs.

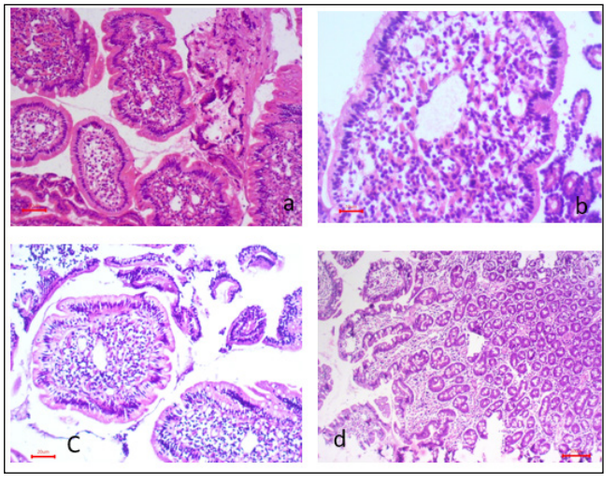

Fig. 5: Histopathologic findings of duodenum H&E stain

(a) 20x mild lymphoplasmacytic infiltration; **(b)** 40x moderate MNC infiltration with goblet cell hyperplasia **(c)** 20x Mild MNC infiltration; **(d)** 10x – erosion with MNC infiltration in the lamina propria with goblet cell hyperplasia

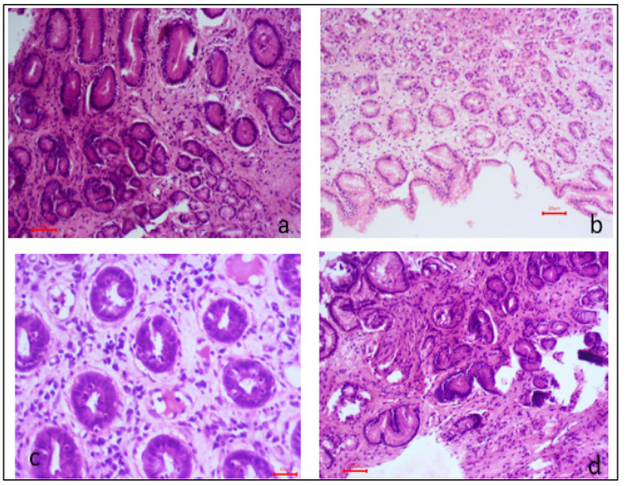

Fig. 6: histopathologic c findings of stomach

(a) 20x fibrosis in between the glands with MNC infiltration; **(b)** 20x mild MNC infiltration, erosion with goblet cell hyperplasia **(c)** 40x severe MNC infiltration; **(d)** 20x – MNC infiltration with piling of nuclei in the lamina propria

Erosions, hyperaemia and discolouration were noticed in entire GI mucosa of CIE affected dogs.

On histopathology, the major inflammatory changes were lymphoplasmacytic infiltration in the lamina propria. However, in one case neutrophil infiltration was noticed along with lymphoplasmacytic infiltration. Majormorphological changes such as surface epithelial injury and goblet cell hyperplasia were observed in the both gastric and duodenal mucosa of CIE affected dogs. Fibrosis of the gastric glands and lacteal dilation of the duodenal mucosa were also recorded. Degeneration, necrosis and the fibrosis in between the crypts of colonic mucosa were recorded in this study (Fig. 5,6 and 4c&d). Similar findings were recorded in the IBD dogs by various authors (Jergens *et al*., 2003; Procoli *et al*., 2013). Villus blunting, fibrosis of the propria, crypt lesions and goblet cell hyperplasia were the morphological abnormalities observed in CIE dogs by the Galler *et al*. (2022) and Perez- Merino *et al*. (2022).

Histopathology of endoscopic guided mucosal biopsy is the gold standard diagnosis for chronic inflammatory enteropathy. The WSAVA International Gastrointestinal Standardization Group developed a histopathological - standards, in the form of text and pictorial templates which might be applied by diagnostic histopathologists in any country with the use of light microscopy and HE-stained sections (Day *et al*., 2008).

Fig. 7: Faecal scoring of CIE

(a) Grade 5- watery diarrhoea; **(b)** Grade 4- poor in consistency with viscous; **(c)** Grade 4.5-liquid stool with semi solid consistency; **(d)** Grade 2-well formed, does not leave a mark when picked up

The presence of lymphoplasmacytic or eosinophilic infiltration in the intestines or a combination of both is

considered as characteristic feature of chronic enteropathy (Wennogle *et al*., 2017). The findings of the study were in the accordance with Jergens *et al*. (2010) and Suchodolski *et al*. (2012) who found similar mucosal infiltration in the IBD dogs.

In the present study, CIE dogs were subjected for the treatment trail. Out of 13 dogs 4 dogs were categorised into food responsive enteropathy (FRE), one was antibiotic responsive enteropathy (ARE), six were in steroid responsive enteropathy (SRE), and 2 dogs in non-responsive enteropathy (NRE) based on the response to treatment.

CONCLUSION

The results of this study suggest that there were no major changes noticed in the endoscopic and histopathologic evaluation in different categories of CIE dogs. Monitoring faecal scoring in CIE will be helpful in assessing the progression of the condition and effectiveness of treatment. However, it may not provide definitive diagnosis to the veterinarians, usually associated with other diagnostic tests. In conclusion, Endoscopy and histopathologic assessment will give the definitive diagnosis for CIE in dogs.

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