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Research article

Characteristic clinical signs and blood parameters in cats with Feline Infectious Peritonitis

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Abstract

Feline infectious peritonitis (FIP) is a common disease with high mortality rates in cats that occurs as either an effusive or non-effusive form. Confirmation of FIP in clinical practice is difficult and remains a challenge because there are no pathognomonic lesions or specific diagnostic indicators. Thus, clinical features were investigated to evaluate the hematological and biochemical parameters between FIP and non-FIP cats. A sample of 50 blood donor cats and 50 effusive FIP cats presented at the Kasetsart University Veterinary Teaching Hospital were divided into non-FIP and FIP groups, respectively. The average age of FIP cats was significantly (p < 0.05) lower than for non-FIP cats. The results indicated that cat breeds correlated with FIP (p < 0.05). Significant results concerning hematological and biochemical findings revealed values of packed cell volume (PCV), red blood cells (RBC), hemoglobin (HGB), mean corpuscular volume (MCV), lymphocytes, eosinophils, blood urea nitrogen (BUN), creatinine, alanine aminotransferase (ALT), albumin and albumin:globulin (A:G) ratio in the FIP group were lower and numbers of white blood cells (WBC), segmented neutrophils, plasma protein (PP), total protein and globulin in the FIP group were higher than in the non-FIP group (p < 0.05). In conclusion, anemia, neutrophilia, lymphopenia, hypoalbuminemia, hyperglobulinemia and a low A:G ratio presented as hematological and biochemical changes in FIP cats. Blood profiling could be a useful approach for FIP diagnosis to assist clinicians to determine and evaluate the correct treatment, prognosis and progressive monitoring.

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Introduction

Feline coronavirus (FCoV) is composed of two clinical biotypes. The first is feline infectious peritonitis virus (FIPV) which is a virulent form of FCoV and the disease usually causes lethal conditions (Addie, 2011). The second is feline enteric virus (FECV) which is a nonvirulent form of FCoV and is associated with asymptomatic persistent enteric infections (Addie et al., 2009). However, FECV infection is highly prevalent in domestic cats worldwide, characterized by subclinical or mild gastroenteritis, while FIPV infection is more severe through induced inflammation, fibrinous to granulomatous serositis and immune-mediated vasculitis (Kipar et al., 2005; Addie, 2011). There are two main forms of FIP known as effusive and non-effusive. A recent study reported that cats with effusive FIP showed shorter clinical onset and survival times than cats with noneffusive FIP (Pedersen, 2009). Cats of any age can develop FIP, with kittens and cats under 2 yr at greater risk (Addie, 2011; Pedersen, 2014; Riemer et al., 2016).

Blood is a specialized body fluid, and measurement of the blood profile is important to evaluate the health status of patients (Simsek et al., 2014). Hematological and biochemical abnormities are often found in cats with FIP; however, the changes are not representative of the disease (Hartman, 2017). Many authors have studied clinicopathological findings in FIP but data from Thailand remain scarce. Typically, cats with FIP have fluid accumulation in body cavities, weight loss, anemia, lymphopenia and decreased serum albumin and elevated serum globulin levels (Norris et al., 2005; Tsai et al., 2011). Several retrospective studies reviewed that FIP is more frequent in young age, male sex and some purebred cats probably predisposed to disease development (Norris et al., 2005; Sharif et al., 2009; Tsai et al., 2011; Worthing et al., 2012; Riemer et al., 2016). In the current study, clinical findings were investigated to determine and evaluate hematological and biochemical parameters as indicators between effusive FIP and clinically healthy (non-FIP) cats.

Materials and Methods

Animal experiments and study design

All experiments were conducted on cats randomly selected by age, gender and breed. The cats were obtained from the Kasetsart University Veterinary Teaching Hospital, Bangkok, Thailand. Blood samples were collected from 100 cats made up of 50 blood donor cats and 50 diagnosed with effusive FIP as non-FIP and FIP groups, respectively. Blood donor cats consisted of clinically healthy cats with no history of FIP exposure. Selection criteria for FIP cats included medical history, clinical appearance, radiography or ultrasonography or both of fluid accumulation in body cavities, cytological examination of the effusion with inflammatory cells, especially macrophages and neutrophils as a modified transudate, and a highly positive result from a feline coronavirus antibody test kit (ImmunoComb®; Biogal Galed Laboratories; Israel). Cats were also screened serologically for feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV) using

the test kit (Witness® FeLV/FIV; Zoetis; USA) with negative results in both FIP and non-FIP cats.

Blood samples for complete blood count (CBC) were collected in tubes containing ethylenediaminetetraacetic acid. Serum specimens for biochemical analysis were collected in non-coagulation tubes. Hematological and biochemical analyses were performed using an automated hematology analyzer (CELL-DYN 3700; Abbott Laboratories; USA) and an automated chemical analyzer (ILab 650; Werfen; India).

Statistical analysis

All statistical analyses were performed using standard software (NCSS 2007 version 07.1.21; Utah; USA). Age and hematological and biochemical parameters were compared using a Student's t test. Breed and gender were analyzed using a χ^2 test. Results were considered significant if p < 0.05 and highly significant if p < 0.001.

Ethics statements

This study was approved by the Ethics Committee of Kasetsart University (ID# ACKU 60-VET-021).

Results

FIP cats were highly significantly younger (median 1.2 yr; mean 2.6 yr; range 0.3–15 yr) compared with non-FIP cats (median 3 yr, mean 3.2 yr; range 1–6 yr). Samples were collected from 32/50 (64%) domestic short-hair (DSH), 8/50 (16%) Persian, 6/50 (12%) Scottish fold, 2/50 (4%) British shorthair, 1/50 (2%) American wirehair and 1/50 (2%) exotic shorthair in the FIP group and 44/50 (88%) DSH, 2/50 (4%) Scottish fold, 2/50 (4%) Persian and 2/50 (4%) American wirehair cats in the non-FIP group. A χ^2 test was performed and a significant relationship was found between breed and the disease. In total, 33/50 (66%) of the cats were male and 17/50 (34%) female in the FIP group, with 35/50 (70%) male and 15/50 (30%) female in the non-FIP group. There was no significant difference in gender distribution between the two groups.

Recorded clinical signs are listed in Table 1. FIP cats presented abdominal distension (68%), depression (60%), dehydration (58%), anorexia (54%), dyspnea (42%), jaundice (24%), diarrhea (4%) and vomiting (2%). Effusion in effusive FIP cats was determined at 33/50 (66%) in the abdomen, 16/50 (32%) in the thorax and 1/50 (2%) in both sites (Table 2).

The hematological findings revealed significant results. Packed cell volume (PCV), red blood cells (RBC), hemoglobin (HGB), mean corpuscular volume (MCV), lymphocytes and eosinophils in FIP cats were all lower than for non-FIP cats but numbers of white blood cells (WBC), segment neutrophils and plasma protein (PP) in FIP cats were higher compared to non-FIP cats (p < 0.05). Values of hematology in FIP cats decreased in PCV, HGB and lymphocytes, increased in segmented neutrophils and PP compared to the reference interval (Table 3). PCV reference intervals were used to diagnose

anemia. Anemia was detected in cats with FIP. In total, anemic cats, 26/50 (52%) had mild anemia (PCV 20-29%), 4/50 (8%) had moderate anemia (PCV 15-19%) and no cats had severe anemia (PCV less than 15%) (data not shown).

The biochemical findings revealed significant results. Values of blood urea nitrogen (BUN), creatinine, alanine aminotransferase (ALT), albumin and the albumin: globulin (A:G) ratio in FIP cats were lower than in non-FIP cats but total protein and globulin were higher (p < 0.05) compared with non-FIP cats. FIP cats showed decreased BUN, creatinine and albumin but increased globulin compared to the reference interval (Table 4).

Discussion

A worldwide survey demonstrated that kittens and cats less than age 2 yr were most likely to develop FIP (Addie, 2011). In the current study 70% of FIP cats were aged less than 2 yr. It has been revealed that purebred cats are highly represented in FIP (Norris et al., 2005; Worthing et al., 2012), while Tsai et al. (2011) reported no significant difference between purebred and DSH. In the current study, cat breeds were correlated to FIP and the percentage of purebred cats in the FIP group (17/50, 34%) showed higher prevalence than the non-FIP group (6/50, 12%). The current results mostly concurred with Tsai et al. (2011) that high populations observed in purebred cats with FIP were Persians and Scottish folds in Taiwan. This finding differed from figures reported in North America and Australia suggesting that Persians were under-represented in FIP (Norris et al., 2005; Pesteanu-Somogyi et al., 2006; Worthing et al., 2012). Examination of the predisposition of specific breeds in previous studies suggested that an important factor for pedigree cats is residing or starting life in a multi-cat environment (Pesteanu-Somogyi et al., 2006; Worthing et al., 2012). Although no risk was associated with gender between FIP and non-FIP groups, the number of male cats within the FIP group (33/50, 66%) was higher than females (17/50, 34%) and FIP was reported to occur more often in male cats (Riemer et al., 2016).

Table 1 Physical and clinical characteristics in cats with effusive feline infectious peritonitis (FIP)

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Clinical sign	Score for FIP cats
Depressed	30/50 (60%)
Anorexia	27/50 (54%)
Dehydrate	29/50 (58%)
<5%	3/50 (6%)
5%	22/50 (44%)
>5%	4/50 (8%)
Dyspnea	21/50 (42%)
Vomiting	1/50 (2%)
Diarrhea	2/50 (4%)
Jaundice	12/50 (24%)
Abdominal distension	34/50 (68%)

Table 2 Distribution of effusion in cats with effusive feline infectious peritonitis (FIP)

Site of fluid accumulation	Score for effusive FIP cats
Abdomen (peritoneal effusion)	33/50 (66%)
Thorax (pleural effusion)	16/50 (32%)
Both thorax and abdomen	1/50 (2%)

Measurement	Reference	Thite		FIP cats			Non-FIP cats		enley a
	interval	CHILD	Mean ± SD	Median	Range	Mean ± SD	Median	Range	p-value
PCV	30.0-45.0	%	28.03 ± 6.74	26.20	15.30-43.50	40.53 ± 3.62	40.25	35.20-48.00	< 0.001
RBC	5.0-10.0	X106/cumm	6.63 ± 1.85	6.58	2.77-11.00	8.35 ± 0.99	8.15	6.76–11.70	< 0.001
HGB	10.0-15.0	%mg	9.10 ± 2.25	8.37	5.02-15.30	13.30 ± 1.13	13.25	11.40–15.90	< 0.001
MCV	39.0–55.0	FI	43.94 ± 7.38	43.59	30.21–66.06	49.23 ± 4.13	49.88	37.85–55.35	< 0.001
MCHC	30.0–36.0	%mg	32.45 ± 1.40	32.52	28.74-36.20	32.75 ± 1.26	32.56	30.17–37.98	0.46
WBC	5.5-19.5	$x10^3/ul$	16.16 ± 8.99	13.80	3.23-41.80	10.90 ± 3.31	9.27	4.81–18.30	0.001
Band neutrophils	0.0-300.0	$x10^3/ul$	0.07 ± 0.02	0.00	0.00 - 1.25	0	0.00	0	0.72
Segmented neutrophils	2.5-12.5	$x10^3/ul$	14.37 ± 9.16	12.47	3.00–36.37	6.91 ± 2.81	6.14	2.57–13.49	< 0.001
Lymphocytes	1.5-7.0	$x10^3/ul$	1.25 ± 1.18	98.0	0.08-4.00	2.26 ± 1.15	2.30	0.29-5.99	< 0.001
Monocytes	0.0-0.9	$x10^3/ul$	0.36 ± 0.61	60.0	0.00-2.74	0.32 ± 0.39	0.15	0.00 - 1.4	0.87
Eosinophils	0.0-0.8	$x10^3/ul$	0.11 ± 0.28	0.00	0.00 - 1.51	0.53 ± 0.53	0.41	0.00 - 3.24	< 0.001
PLT	300.0-800.0	$x10^3/ul$	308.98 ± 145.34	300.00	50.00-837.00	304.40 ± 90.30	300.00	191.00-520	0.55
PP	6.0-7.5	%mä	8.11 ± 1.49	7.80	6.20-12.00	7.28 ± 1.55	7.10	9.8-00.9	0.02

PCV = packed cell volume; RBC = red blood cells; HGB = hemoglobin; MCV = mean corpuscular volume; MCHC = mean corpuscular hemoglobin concentration; WBC = white blood cells; PLT = platelets; p-value of < 0.05 and <0.001 indicate a significant difference and a highly significant difference, respectively, between the FIP and non-FIP groups.

 Table 4
 Comparison of biochemical values between feline infectious peritonitis (FIP) and non-FIP groups

Measurement	Reference	Traite		FIP cats			Non-FIP cats		. Volue
	interval	CIIIIS	Mean ± SD	Median	Range	Mean ± SD	Median	Range	p-value
BUN	19.0–34.0	mg%	17.34 ± 8.43	16.00	8.00-55.00	24.58 ± 4.27	24.00	16.00–35.00	< 0.001
Creatinine	0.9–2.2	mg/dL	0.86 ± 0.31	0.82	0.31-1.59	1.51 ± 0.31	1.50	1.06 - 2.06	< 0.001
ALT	25.0–97.0	IU/L	52.00 ± 45.55	37.00	7.00–261.00	69.52 ± 30.70	57.50	41.00-185.00	< 0.001
TP	6.0-7.9	mg/dL	7.94 ± 1.68	7.65	5.20-11.50	7.70 ± 0.76	7.60	6.10-9.60	0.006
Albumin	2.8–3.9	%mg	2.28 ± 0.37	2.30	1.60 - 3.10	3.51 ± 0.30	3.50	2.89-4.00	< 0.001
Globulin	2.6-5.1	$x10^3/ul$	5.66 ± 1.54	5.35	3.50-9.00	4.19 ± 0.81	4.15	2.90-6.10	< 0.001
A:G ratio	ı	ı	0.43 ± 0.12	0.43	0.21 - 0.68	0.87 ± 0.20	0.85	0.54-1.26	< 0.001

p-value of < 0.05 and <0.001 indicate a significant difference and a highly significant difference, respectively, between the FIP and non-FIP groups BUN = blood urea nitrogen; ALT = alanine aminotransferase; TP = total protein; A:G ratio = albumin:globulin ratio.

As previously reported, the clinical presentations in FIP cats depend on pyogranulomatous inflammation which damages the organs (Addie, 2011). The current results indicated that the most common clinical features in FIP cats were abdominal distension (68%), depression (60%), dehydration (58%), anorexia (54%) and dyspnea (42%). Effusive FIP is presented with abdominal, pleural and/or other body cavities (pericardial cavities, renal subcapsular space, scrotum, etc.) effusions due to an increase in the vascular permeability caused by blood vessel inflammation (Takano et al., 2011). Cats can present dyspnea or abdominal distension or both (Kipar et al., 2005; Ettinger et al., 2017; Tasker, 2018). According to the clinical findings, hydration status may affect the interpretation of blood parameter results. It has been reported that PCV, HGB and plasma protein concentration increase in dehydrated patients (Nose et al., 1983; Ashraf and Rea, 2017) which may interfere with some hematological and biochemical values including total protein and albumin levels (Ashraf and Rea, 2017). Of these reasons, the clinician should be aware of the hydration status before interpreting the laboratory results. Here, approximately 25% of the FIP cats presented jaundice. Recent studies reported jaundice as a clinical finding in FIP, mostly found in effusive types (Tasker, 2018). Some clinical aspects including neurological signs (ataxia, paresis, seizure, hyperesthesia, behavior changes) have been presented in FIP (Foley et al., 1998; Norris et al., 2005) but these clinical features were not observed in the current study. Foley et al. (1998) utilized magnetic resonance imaging, polymerase chain reaction and serology to diagnose neurological FIP. Their results showed that cats with neurological FIP had focal lesions, relatively small amounts of virus in the brain tissue and some extensive histopathological changes. Both forms of FIP are associated with neurological abnormalities but non-effusive FIP is more commonly found (Tasker, 2018). These representations suggested that further observational studies should be performed to improve misdiagnosis in clinical practice.

Hematological findings often show changes in cats with FIP but may not be specific enough to identify the disease (Hartmann, 2017). Pedersen (2014) considered that common abnormalities in FIP usually include non-regenerative anemia, leukocytosis in cases of increased absolute neutrophil count, decreased absolute lymphocyte count, elevated serum protein and a low A:G ratio. In the current study, 60% (30/50) of cats with FIP were anemic, correlating with Sparkes et al. (1991) who reported that 60% of FIP-diseased cats presented anemia. The current study determined neutrophilia in FIP. Takano et al. (2009) suggested two main issues: 1) an increase in the tumor necrotic factor-alpha, granulocyte-macrophage colony-stimulation factor and granulocyte colony stimulating factor release from FIPV-infected macrophages and 2) these cytokines contribute to prolong neutrophil survival. Moreover, these three cytokines are involved in the formation of granulomatous lesions (Takano et al., 2011). In the current clinical study, lymphopenia was observed in FIP cats. This result agreed with Addie (2011) who described lymphopenia as a consistent feature of naturally infected FIP. In addition, lymphopenia was considered in both effusive and non-effusive FIP and caused T lymphocyte cell depletion by virus-induced T-cells apoptosis (Haagmans et al., 1996;

Paltrinieri et al., 2001).

In the current study, lower BUN and creatinine levels were observed in FIP cats. Backlund et al. (2011) reported that dietary intake affected BUN and several other biochemical parameters. The authors expected that anorexia in FIP cats might lead to inadequate nutrition, weight loss and reduced muscle mass which then contributed to lower BUN and creatinine levels in cats with FIP. An abnormal BUN level is often associated with kidney disease and/or impaired liver function (Trotman et al., 2007; Cannon, 2016). The disruption of urea cycle in cats may result from arginine deficiency that contributes to low levels of urea (Morris and Rogers, 1978). Moreover, the inflammation of the intestinal area in cats with FIP can limit the ability to absorb protein from food that might be a cause of the low BUN levels (Dimski, 1994; Eckersall, 2008). Hyperproteinemia often presents as a common laboratory abnormality in cats with FIP as a result of hyperglobulinemia, mainly gamma globulins, or hypoalbuminemia or both (Hartmann et al., 2003; Ettinger et al., 2017). In the current study, an increase in the total protein level in FIP cats was not observed but hyperglobulinemia and hypoalbuminemia levels were found. Riemer et al. (2016) reported that only 17.5% of cats with FIP showed hyperproteinemia and that increase in serum total protein was less likely in effusive than in non-effusive FIP. All cats in the FIP group had a lower A:G ratio, 60% (30/50) of FIP cats had a value less than 0.4 and 40% (20/50) of cats had a value in the range 0.5-0.7. Hartmann et al. (2003) reported an optimal cut-off value of 0.8 for the A:G ratio in the disease. Many previous studies suggested an A:G ratio of less than 0.4 which makes FIP occurrence very likely, while an A:G ratio of more than 0.8 makes FIP occurrence very unlikely (Tsai et al., 2011; Tasker, 2018). However, a decreased A:G ratio could be due to the high levels of serum globulins that are also detected in chronic inflammatory diseases, immune system disorders and some tumors (Eckersall, 2008). A study of electrophoretograms in feline diseases revealed that most FIP cats had increased gamma globulins and polyclonal gammopathies were considered in FIP cases which was different from feline lymphoma where a monoclonal gammopathy is more common (Taylor et al., 2010). The A:G ratio in the current study was the strongest biochemical parameter, indicating dysproteinemia in FIP which lends further support to previous studies (Norris et al., 2005; Riemer et al., 2016; Tasker, 2018).

At present, there is no effective treatment. The recommended treatment for the disease is to suppress the inflammatory and immune response using drugs such as prednisolone. Vasculitis is usually treated by giving pentoxifylline to FIP cats. (Fischer et al., 2011; Pedersen, 2014). The clinicians should monitor for concurrent illness including secondary bacterial infections, starvation and anemia. In severe anemic FIP cats, erythropoietin or darbepoetin and a blood transfusion might be considered (Chalhoub et al., 2012). Supportive treatments also may include draining accumulated fluids, fluid therapy to correct dehydration, feeding tube administration and dietary supplements such as vitamins, amino acids and antioxidants to support health and nutrition status (Diaz and Poma, 2009). The prognosis for cats with FIP is poor to grave (Hartmann, 2009; Pedersen, 2014). Although, there is no cure for FIP cats, some cats can survive longer and have

a better quality of life with symptomatic treatment (Ettinger et al., 2017).

The current study was the first analysis of clinical and laboratory findings for FIP in Thailand. Age and cat breeds were found to be predisposing factors of FIP. Obvious clinical features included abdominal distension and dyspnea, with changes in hematological and biochemical values commonly found in FIP. Some aspects of the current study concurred with research results in Asia but differed with results from Australia, Europe and North America. To ascertain the tendency of FIP worldwide, more detailed investigation is required of reports of prevalence and clinicopathologic features of FIP in Thailand and other countries in Asia.

Conflict of Interest

The authors declare that there are no conflicts of interest.

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