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Friederike Riemer, Kirsten A. Kuehner, Susanne Ritz, Carola Sauter-Louis ...+1 more authors

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Clinical and laboratory features of cats with feline infectious peritonitis – a retrospective study of 231 confirmed cases (2000–2010)

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Friederike Riemer¹, Kirsten A Kuehner¹, Susanne Ritz¹,
Carola Sauter-Louis² and Katrin Hartmann¹

Abstract

Objectives The objectives of this study were to review signalment, clinical signs and laboratory features in a large number of naturally occurring cases of feline infectious peritonitis (FIP), and to evaluate potential changes in diagnostic criteria for FIP and compare findings in cats with and without effusion.

Methods The medical records of 231 cats with confirmed FIP that presented to the Clinic of Small Animal Medicine of the Ludwig-Maximilian University of Munich, Germany, were reviewed for signalment, history, and clinical and laboratory parameters. Age, sex and breed distribution of the cats were compared with the clinic population.

Results Male sex and young age were significantly correlated with FIP. Neutering status was not associated with FIP. No breed predisposition was observed and the majority of cats presented were domestic shorthair and mixed breed. Microcytosis of peripheral erythrocytes was found in 35.1% of cats, of which 42.4% did not have concurrent anaemia. Band neutrophilia was documented in 44.3% (81/183), of which 35.8% did not have mature neutrophilia. Lymphopenia, observed significantly more often with effusion, was documented in only 26.8% of cats without effusion. Hyperbilirubinaemia also occurred significantly more often in cats with vs without effusion. While serum total protein was increased in only 17.5% of cats, hyperglobulinaemia was documented in 89.1%. Nearly 85.0% of cats had an albumin-to-globulin (A:G) ratio <0.8, while 67.8% had an A:G ratio <0.6.

Conclusions and relevance Microcytosis was common and can increase suspicion of FIP in the presence of other typical clinical and laboratory abnormalities. The low prevalence of lymphopenia in cats without effusion suggests that this is not a useful parameter in non-effusive FIP. The frequent occurrence of a left shift in the absence of a mature neutrophilia complicates the differentiation of effusive FIP and septic peritonitis. Globulins and A:G ratio were of higher diagnostic value than hyperproteinaemia.

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Introduction

Feline infectious peritonitis (FIP) is a worldwide disease of domestic and wild felids caused by the virulent biotype of feline coronavirus (FCoV), sometimes referred to FIP virus (FIPV).^{1–3} It has been reported that mainly young cats aged 6 months to 2 years and male cats are affected.^{4–10} Furthermore, some breeds are thought to be predisposed to developing FIP.^{6–12} Clinical signs are mainly non-specific, such as recurrent fever, anorexia, chronic weight loss, and central nervous system (CNS) signs or ocular changes.^{4,13} Effusion can occur in visceral cavities due to serositis.¹⁴ Ante-mortem diagnosis of FIP is challenging as there are no pathognomonic clinical signs or laboratory changes. The examination of effusion

by the use of immunofluorescence staining of FCoV antigen in macrophages is highly specific but is complicated by the often low numbers of macrophages in the effusion

¹Clinic of Small Animal Medicine, Ludwig-Maximilian University, Munich, Germany

²Clinic for Ruminants with Ambulatory and Herd Health Services, Ludwig-Maximilian University, Munich, Germany

Corresponding author:

Friederike Riemer, Clinic of Small Animal Medicine, Ludwig-Maximilian University, Veterinärstrasse 13, 80539 Munich, Germany
Email: friederike.riemer@gmail.com

and, also, is of no use in those cats without effusion.^{15,16} While immunohistochemical staining can also be applied to organ biopsy specimens, FIP is generally considered substantially more difficult to diagnose definitively in vivo in cats without vs with effusion as clinical signs and laboratory features are more vague.¹⁶

Several studies have looked at clinical and laboratory abnormalities in cats with FIP. However, most of these studies contained either a smaller number of cats or only evaluated signalment.^{4–10,17–20} In addition, the last data from Europe were published almost 20 years ago.^{4,19} Therefore, the aims of the study were to re-examine signalment, and clinical and laboratory features in a large group of cats with confirmed FIP and to compare findings in those cats with and without effusion evaluating differences in clinical and laboratory parameters.

Materials and methods

Selection of cases

This study retrospectively evaluated the medical records in the computerised database of the Clinic of Small Animal Medicine (CSAM) of the Ludwig-Maximilian University, Munich, Germany, between 2000 and 2010. Out of 16,715 cats registered in the CSAM between 1 January 2000 and 15 September 2010, 231 cats with a definitive diagnosis of FIP were identified. A diagnosis of FIP was considered definitive if (1) immunofluorescence staining of effusion revealed FCoV antigen in macrophages ($n = 38$),¹⁵ or (2) tissue samples collected during necropsy ($n = 185$) or surgery ($n = 8$) showed histological lesions characteristic of FIP.^{21–25} Signalment, history, results of the clinical examination and laboratory results were obtained from the medical records. Fever was classified as temperature $>39.0^{\circ}\text{C}$. In some statistical tests a cutoff of $\geq 39.5^{\circ}\text{C}$ was selected in an attempt to exclude cats with stress-induced hyperthermia.

Statistical analysis

Statistical analysis was performed using commercial software (SPSS Version 18 [IBM]; StatCalc 5.4.1). Descriptive statistics were performed for all evaluated variables. Categorical data were analysed using a χ^2 test. In 2×2 contingency tables with any expected cell values < 5 , Fisher's exact two-tailed results were used. Additionally, the Mann-Whitney test was used to compare non-categorical data between groups. Age, sex, reproductive status and breed distribution of cats with FIP were compared with the feline clinic population presented to the CSAM from 1 January 2000 to 15 September 2010. History, clinical signs and laboratory parameters were compared within the group of cats with FIP. A Bonferroni correction was performed to rule out multiple test interference, and $P \leq 0.01$ for each individual parameter was considered significant. A multivariate analysis was used to compare age, sex and neutering status.

Results

Signalment

Cats with FIP were significantly younger than the clinic population ($P < 0.001$) and FIP occurred significantly more often in cats younger than 2 years of age ($P < 0.001$). In contrast, cats with FIP older than 7 years were significantly under-represented ($P < 0.001$) when compared with the clinic population (Table 1). Male sex was significantly associated with FIP ($P < 0.001$) (Table 1). The age of cats with FIP ranged from 2 weeks to 19 years (median 1.5 years, mean 3.7 years, interquartile range [IQR] 5.0) and did not differ significantly between males (median 1.8 years, mean 4.2 years, IQR 6.0) and females (median 1.0 years, mean 2.7 years, IQR 2.8). When controlling for age, the reproductive status of neither sex was associated with disease. Purebred cats were not over-represented when compared with the clinic population.

History

Where the housing density was recorded in the clinical record, almost two-thirds of cats with FIP (107/158; 65.9%) lived in a single- or two-cat household at the time of diagnosis; 59.9% (100/167) were indoor cats, while 40.1% (67/167) were permitted to roam outdoors. Specific stressful events preceding diagnosis were documented for 131/231 cats (Table 2).

Clinical signs

The clinical signs that were documented are listed in Table 3. On history, fever ($\geq 39.0^{\circ}\text{C}$) was documented in 55.8% (120/215) of cats with FIP. Of the 111 cats with FIP for which the temperature was documented on physical examination, the majority (91/111; 81.0%) had a temperature above 39.5°C , with nearly half ($n = 43$) of these cats being severely pyrexic with a temperature $> 40^{\circ}\text{C}$. Cats with CNS signs were less likely to have fever $\geq 39.5^{\circ}\text{C}$ (odds ratio 0.031, 95% confidence interval 0.12–0.77; $P = 0.005$) than those without CNS signs. Effusion was detected in 78.1% (175/224) of cats with FIP. Of these, the majority (78.3%; 137/175) had ascites. Cats with effusion were significantly more likely to have fever $\geq 39.0^{\circ}\text{C}$ and less likely to have CNS signs (Table 3).

Haematology

Haematological changes were observed in nearly every cat (99.5%; 199/200) (Table 4). Severe anaemia, classified as a haematocrit $\leq 10\%$, was uncommon and documented in only five cats (4.7%). Two of these five cats had reticulocytosis and hyperbilirubinaemia consistent with haemolytic anaemia. Microcytosis was detected in more than one-third of cats with FIP (35.1%; 66/188). Over 40% of these cats were not anaemic (28/66; 42.4%). Microcytosis was not associated with anaemia ($P = 0.445$) or age ($P = 0.225$). Lymphopenia was recorded in

Table 1 Signalment of cats with feline infectious peritonitis (FIP) compared with the clinic population

	Cats with FIP (n = 231)	Clinic population (n = 16,275)	P value*	OR (95% CI)
Sex				
Male	151 (65.4)	8849 (54.4)	<0.001	1.58 (1.20–2.10)
Intact	57 (24.7)	2065 (12.7)		
Neutered	94 (40.7)	6778 (41.7)		
Female	80 (34.6)	7426 (45.6)		
Intact	42 (18.2)	2275 (14.0)		
Spayed	38 (16.4)	5145 (31.6)		
Age groups (years)	n = 222	n = 15,724		
<1	87 (39.2)	1986 (12.6)	<0.001	4.46 (3.36–5.91)
≥1–2	33 (14.9)	927 (5.9)	<0.001	2.79 (1.88–4.11)
>2–4	32 (14.4)	1895 (12.1)		
>4–7	25 (11.3)	2189 (13.9)		
>7–11	16 (7.2)	3277 (20.8)	} <0.001	0.19 (0.14–0.27)
>11	29 (13.1)	5450 (34.7)		
Breed	n = 229	n = 15,685		
DSH/mixed	185 (80.1)	12,356 (78.8)		
Persian	9 (3.9)	926 (5.9)		
Maine Coon	7 (3.1)	720 (4.6)		
Birman	6 (2.6)	106 (0.7)		
British shorthair	5 (2.2)	296 (1.9)		
Siamese	4 (1.7)	323 (2.1)		
Chartreux	4 (1.7)	106 (0.7)		
NFC	4 (1.7)	224 (1.4)		
Oriental shorthair	2 (0.9)	45 (0.3)		
Devon Rex	2 (0.9)	12 (0.1)		
Sphynx	1 (0.4)	1 (0.0)		

Data are given as n (%)

*Significance $P \leq 0.01$ (χ^2 test). OR = odds ratio; CI = confidence interval; DSH = domestic shorthair; NFC = Norwegian Forest Cat

Table 2 Frequency of documented stress situations and keeping conditions of cats with feline infectious peritonitis (FIP)

	Animals
Stress (n = 131)*	
Adoption	38 (29.0)
Animal shelter	31 (23.7)
Surgery	29 (22.1)
Upper respiratory tract disease	12 (9.2)
Vaccination	9 (6.9)
Household with other cats with FIP	8 (6.1)
Boarding	6 (4.6)
Breeding	6 (4.6)
New cat in household	4 (3.0)
Ran away	1 (0.8)
Keeping condition (n = 167)	
Indoor	100 (59.9)
Outdoor	67 (40.1)
Housing density (n = 158)	
Single cat	29 (18.3)
1 cat	75 (47.5)
2 cats	20 (12.7)
3 cats	7 (4.4)
>3 cats	27 (17.1)

Data are given as n (%)

*Some cats had multiple stressors

49.5% of cats with FIP (89/184) and was observed significantly more often in cats with effusion (Table 5). Band neutrophilia ($>500/\mu\text{l}$) was documented in 44.3% (81/184) of cats with FIP. More than one-third of cats with a left shift (35.8%; 29/81) did not have a simultaneous elevation in segmented neutrophils. There was no correlation between fever ($>39.9^\circ\text{C}$) and either mature ($P = 0.588$) or band neutrophilia ($P = 0.895$).

Serum biochemistry

Changes on the serum biochemistry profile were observed in 99.5% (186/187) of cats with FIP (Table 5). Elevated serum bilirubin was significantly more common in cats with effusion (Table 6), and there was no correlation with elevated liver enzymes ($P = 0.233$). Over one-third of cats with hyperbilirubinaemia had an anaemia without elevated liver enzymes (38/109; 34.9%). Hyperproteinaemia was documented in only 17.5% (32/183) of cats with FIP. An increase in serum total protein was significantly less likely in cats with effusion than in cats without effusion. Hyperglobulinaemia, documented in 89.1% (163/183) of cats, was not significantly associated with effusion. Nearly 85.0% (155/183) of cats with FIP had an albumin:globulin (A:G) ratio <0.8 , while 67.8% (124/183) of cats had an A:G ratio <0.6 . A:G ratios

Table 3 Historical and physical findings in cats with feline infectious peritonitis and the correlation with having effusion

Clinical signs	n (%)	Association with effusion		
		With effusion, n (%)	P value*	OR (95% CI)
Distribution of effusion	175/224 (78.1)			
Ascites	137/175 (78.3)			
Thoracic effusion	23/175 (13.1)			
Ascites and thoracic effusion	14/175 (8.0)			
Ascites and pericardial effusion	1/175 (0.6)			
Lethargy, depression	194/222 (87.4)	149/190 (78.4)	0.320	
Inappetence	144/217 (66.4)	113/143 (79.0)	0.490	
Fever (°C)	111/190 (58.4)	99/117 (84.6)	0.004	2.58 (1.26–5.28)
Mild (39.0–39.4)	20/111 (18.0)	77/88 (87.5)	0.019	
Moderate (≥39.5–40.0)	48/111 (42.3)			
Severe (>40.0)	43/111 (38.7)			
Weight loss	82/219 (37.4)	64/80 (80.0)	0.733	
Vomitus, diarrhoea	36/220 (16.4)	28/36 (77.8)	1.000	
Dyspnoea	17/220 (7.7)	14/16 (87.5)	0.534	
Neurological signs	39/221 (17.6)	18/39 (46.2)	<0.001	0.16 (0.07–0.36)
Ataxia	14/39 (35.9)			
Seizures	10/39 (25.6)			
Vestibular syndrome	9/39 (23.1)			
Paresis, paralysis	5/39 (12.8)			
Somnolence	1/39 (2.6)			

*Considered significant if $P \leq 0.01$

OR = odds ratio; CI = confidence interval

did not differ significantly between cats with and without effusion. Low albumin levels were significantly more common in cats with effusion, while azotaemia was detected significantly more often in cats without effusion.

Discussion

This retrospective study examined signalment, history, and the clinical and laboratory features of a large group of cats with confirmed FIP. To our knowledge, comparable studies of a large number of cats with FIP, evaluating signalment, history, clinical signs and laboratory data, have not been performed in the past 20 years in Europe.^{4,19}

As reported previously,^{4,6,7,9,10} this study detected FIP significantly more often in male cats. The role of sex-specific differences in the immune system is still not clear, especially in regard to cell-mediated immunity.⁷ Sex steroid hormones exert influence on cell-mediated immunity by affecting T-cell function.²⁶ Androgens can dampen the immune response,²⁷ which could potentially increase virus multiplication, thereby raising the risk of mutations of the viral genome thought to cause FIP. Consequently, hormonal influences on cell-mediated immunity might play a key role in the development of FIP, explaining the predisposition of male cats observed in multiple studies.^{4,6,7,9,10} Alternatively, sex-linked genes could potentially be responsible for predisposing male cats to FIP. In humans, for example, mutations on the Y chromosome are known to lead to several diseases, such

as hearing impairment or a higher risk of developing coronary artery disease.^{28,29} Genes directly influencing the immune system might also be sex-linked, as demonstrated by an experimental study, which established a mouse strain with Y chromosome-linked hereditary B- and natural killer-cell deficiencies.³⁰

Several studies have found that cats with FIP are significantly more likely to be intact,^{4,6,8,9} especially male cats.^{4,6} Upon adjusting for age, Rohrbach et al observed an over-representation of intact males, while spayed females were under-represented.⁶ They postulated that this was likely due to differences in behavioural patterns of spayed females vs sexually intact male cats.⁶ A higher prevalence of intact male cats with FIP is also consistent with the above hypothesis that sex steroid hormones, specifically androgens, negatively influence immunity. Castrated males produce less androgen and therefore should be less prone to developing FIP. The present study, however, found no correlation between FIP and neutering status in either sex after controlling for age. Perhaps the effect of hormonal status on the development of FIP is counterbalanced by the stress of surgery from neutering. Stress is known to suppress the immune system, thus increasing the risk of FIP via a higher rate of viral replication and risk of mutations.

Interestingly, the majority (65.8%) of cats lived in a single-cat household (18.3%) or together with just one other cat (47.5%) at the time of diagnosis. This is

Table 4 Complete blood cell count of cats with feline infectious peritonitis

Measurement	Reference interval	Animals examined (n)	Range	Mean	Median	Samples within normal interval, n (%)	Samples below normal, n (%)	Samples above normal, n (%)
Packed cell volume (l/l)	0.30–0.44	200	0.07–0.52	0.30	0.29	86 (43.0)	106 (53.0)	8 (4.0)
Mild anaemia	>0.20–0.30	106					85 (80.2)	
Moderate anaemia	0.11–0.20	106					16 (15.1)	
Severe anaemia	≤0.10	106					5 (4.7)	
Red blood cells ($\times 10^{12}/l$)	5.0–10.0	199	1.68–12.80	7.28	7.23	155 (77.9)	24 (12.1)	20 (10.1)
Haemoglobin (mmol/l)	5.6–9.3	199	1.44–28.30	6.26	6.09	124 (62.3)	66 (33.2)	9 (4.5)
Mean cell volume (fl)	40.0–50.0	187	29.20–52.80	41.45	41.70	118 (63.1)	66 (35.3)	3 (1.6)
MCHC (mmol/l)	19.0–22.0	187	0.30–24.80	20.35	20.30	162 (86.6)	10 (5.3)	15 (8.0)
Thrombocytes ($\times 10^9/l$)	180.0–550.0	115	50.00–745.00	258.82	240.00	77 (67.0)	32 (27.8)	6 (5.2)
White blood cell count ($\times 10^9/l$)	6.0–11.0	200	2.02–77.00	17.26	19.10	48 (24.0)	13 (6.5)	139 (69.5)
Monocytes ($\times 10^9/l$)	0.04–0.50	184	0–2.00	0.35	0.24	95 (51.6)	45 (24.5)	44 (23.9)
Lymphocytes ($\times 10^9/l$)	1.0–4.0	184	0–7.76	1.46	1.02	81 (44.0)	91 (49.5)	12 (6.5)
Segmented neutrophils ($\times 10^9/l$)	3.0–11.0	184	0.98–72.38	14.38	12.08	71 (38.6)	8 (4.3)	105 (57.1)
Neutrophilia with left shift		105						52 (49.5)
Neutrophilia without left shift		105						53 (50.5)
Band neutrophils ($\times 10^9/l$)	0–0.6	184	0–8.76	1.01	0.46	103 (56.0)	–	81 (44.0)
Mild left shift	0.6–1.0	81						24 (29.7)
Moderate left shift	>1.0–2.0	81						30 (37.0)
Severe left shift	>2.0	81						27 (33.3)
Basophils ($\times 10^9/l$)	0–0.04	184	0–0.02	0.0001	0	184 (100.0)	–	0 (0)
Eosinophils ($\times 10^9/l$)	0.04–0.06	184	0–5.00	0.09	0	27 (14.7)	150 (81.5)	7 (3.8)

MCHC = mean cell haemoglobin concentration

surprising as housing density is regarded as a major risk factor for FIP.^{16,31–36} A likely explanation is previous exposure to FCoV before the young cats changed from a multi-cat environment into the new household with prolonged carriage of FCoV.

On haematology, microcytosis was detected in over one-third of cats with FIP. Interestingly, 40.0% (27/66) of these cats with microcytosis were not anaemic. Microcytosis is not well described in cats. A study examining blood samples in young cats aged 2–10 weeks detected microcytosis in the 2–4-week-old group. These kittens had lower serum iron and transferrin saturation values.³⁷ Although young cats with FIP were significantly over-represented, in the present study, microcytosis did not correlate with age. In humans, microcytosis is a result of haemoglobinopathies due to iron deficiency, lead toxicity, chronic disease, thalassaemia trait or sideroblastic anaemia.^{38,39} While the microcytosis seen in cats with FIP could potentially be due to iron sequestration caused by chronic disease, anaemia of chronic disease in cats is more commonly associated with normocytic anaemia.⁴⁰ Reduced intestinal iron absorption due to hepcidin is a more likely explanation for FIP-associated microcytosis. This protein that inhibits iron uptake in the gut is

stimulated by interleukin-1 and interleukin-6,⁴¹ which have been shown to be elevated in cats with FIP.^{42–44} As microcytosis with and without anaemia was commonly observed in cats with FIP in the present study, the presence of this laboratory abnormality in a cat with other clinical and laboratory parameters suggestive of FIP can increase the suspicion of this disease.

Lymphopenia, thought to be caused by virus-induced apoptosis of T cells and observed in 49.5% of 126 cats in the present study, is considered the most common haematological abnormality in both effusive and non-effusive FIP.^{16,17,45–47} Whereas Sparkes et al observed no significant difference in the lymphocyte count of cats with effusion vs those without effusion,¹⁹ the present study documented lymphopenia significantly more often in cats with effusion (78/139; 56.1%). Only 26.8% (11/41) of cats without effusion had a reduced lymphocyte count. A possible explanation for the significantly higher prevalence of lymphopenia in cats with effusion could be the perivascular migration of lymphocytes secondary to vasculitis in cats with effusion.^{23,48} This finding suggests that lymphopenia, considered a frequently observed, if non-specific laboratory change in cats with FIP,^{16,47} might not be as common an abnormality in the

Table 5 Serum biochemistry of cats with feline infectious peritonitis

Measurement	Reference interval	Animals examined (n)	Range	Mean	Median	Samples normal, n (%)	Samples below normal, n (%)	Samples above normal, n (%)
ALT (U/l)	0–114.00	165	0–1428.00	76.47	36.00	141 (85.5)	–	24 (14.5)
AST (U/l)	0–63.00	38	8.00–730.00	64.25	25.00	25 (65.8)	–	13 (34.2)
ALP (U/l)	0–94.00	162	2.00–210.00	28.01	17.00	154 (95.1)	–	8 (4.9)
Bilirubin ($\mu\text{mol/l}$)	0–4.74	174	0.40–209.10	23.76	8.02	65 (37.4)	–	109 (62.6)
Mild bilirubinaemia	0–7.99							20 (18.3)
Moderate bilirubinaemia	8.00–15.99							28 (25.7)
Severe bilirubinaemia	>16.00							61 (56.0)
Urea (mmol/l)	5.00–11.30	186	3.05–62.50	8.92	6.73	128 (68.8)	29 (15.6)	29 (15.6)
Creatinine ($\mu\text{mol/l}$)	0–169.00	185	17.00–627.00	89.15	75.00	177 (95.7)	–	8 (4.3)
Total protein (g/l)	57.00–80.00	183	14.10–136.80	76.69	74.00	133 (72.7)	18 (9.8)	32 (17.5)
Albumin (g/l)	26.00–56.00	183	8.20–48.10	24.87	24.00	65 (35.5)	118 (64.5)	0 (0)
Globulins (g/l)	>50.00	183	5.90–117.20	51.78	49.80	20 (11.0)	–	163 (89.0)
Albumin/globulin ratio	<0.80	183	0.15–2.54	0.55	0.50	28 (15.3)	155 (84.7)	–
	<0.60	183	0.15–2.54	0.55	0.50	59 (32.2)	124 (67.8)	–
α_1 -globulin (g/l)	2.00–13.00	47	0.10–8.40	1.81	1.40	19 (40.4)	28 (59.6)	0 (0)
α_2 -globulin (g/l)	4.00–11.00	47	0.70–61.40	9.36	8.50	12 (25.5)	18 (38.3)	17 (36.2)
β -globulin (g/l)	3.00–15.00	47	4.80–29.30	14.24	12.30	28 (59.6)	0 (0)	19 (40.4)
γ -globulin (g/l)	6.00–26.00	47	2.50–101.10	27.86	24.50	21 (44.7)	4 (8.5)	22 (46.8)

ALT = alanine aminotransferase; AST = aspartate aminotransferase; ALP = alkaline phosphatase

Table 6 Significant correlations in cats with feline infectious peritonitis between clinical signs, blood parameters and presence of effusion

	Cats with effusion	Cats without effusion	<i>P</i> value†	OR	95% CI
Clinical signs					
Fever ($\geq 39.0^\circ\text{C}$)	99/163 (60.7)	18/48 (37.5)	0.004	2.58	1.26–5.28
Neurological signs	18/168 (10.7)	21/49 (42.9)	<0.001	0.16	0.07–0.36
Blood parameters					
Lymphocytes ↓	78/139 (56.1)	11/41 (26.8)	0.001	3.49	1.53–8.09
Bilirubin ↑	91/134 (67.9)	15/35 (42.9)	0.006	2.82	1.24–6.48
Urea ↑	17/141 (12.1)	12/39 (30.8)	0.005	0.31	0.12–0.78
Creatinine ↑	2/141 (1.4)	6/39 (15.4)	0.001	0.08*	0.01–0.46
Total protein ↑	19/141 (13.5)	12/36 (33.3)	0.005	3.24	1.28–8.16
Albumin ↓	97/141 (68.8)	20/36 (55.6)	0.007	2.76	1.23–6.22

Data are given as n (%)

*Two-tailed Fisher's exact test used because of small numbers

†Considered significant if $P \leq 0.01$

OR = odds ratio; CI = confidence interval

difficult-to-diagnose group of FIP cats without effusion as previously thought.

A mature neutrophilia, often accompanied by a left shift, is commonly observed in cats with FIP.^{4,17,18} This neutrophilia is most likely due to non-specific reactive changes of the bone marrow, namely neutrophilic granulocyte hyperplasia with a left shift of the granulocytic

series in cats with FIP.⁴⁹ In the present study, band neutrophilia – usually in form of a moderate-to-severe left shift ($>1000/\mu\text{l}$; range 1000–8760/ μl) – was observed in 44.3% (81/184) of cats with FIP. Interestingly, 29/81 cats (35.8%) had a left shift without mature neutrophilia, a finding more commonly expected in cases of septic peritonitis,^{50,51} an important differential diagnosis to FIP in

cats presenting with fever and effusion. In the absence of toxicity, this could potentially complicate the differentiation of effusive FIP from a septic abdomen, especially in cats pretreated with antibiotics.

Similar to former studies, hyperbilirubinaemia, a common serum abnormality in cats with FIP, was mostly moderate-to-severe ($>8.0 \mu\text{mol/l}$; range 8.0–209.1 $\mu\text{mol/l}$).^{4,10,19,20} As expected, high bilirubin values were not correlated with elevated liver enzymes, as hyperbilirubinaemia in cats with FIP is not a reflection of parenchymal liver disease but rather is due to excessive erythrocyte fragility leading to an increased destruction of red blood cells.⁵² The ensuing breakdown products of haemoglobin, bilirubin and biliverdin accumulate as a result of the cat's intrinsically poor glucuronidation capacity.⁵³ Previous studies have reported elevated bilirubin levels in nearly 90% of FIP cats with effusion.^{19,20} In the present study, hyperbilirubinaemia was significantly more common in cats with effusion (91/134; 67.9%) than in cats without effusion (15/35; 42.8%), possibly due to the more severe vasculitis underlying effusive FIP. Inflammation is known to compromise biliary metabolism and excretion in the liver because endotoxins and cytokines cause a decreased gene expression of hepatocellular transporters needed for bile salt transport.⁵⁴ Thus, in patients with inflammation due to sepsis, for example, the basolateral and canalicular transport of bile acids is decreased causing insufficient transport of bilirubin out of the blood.⁵⁵ Finally, although hyperbilirubinaemia is considered one of the cardinal clinical signs of FIP,^{4,10,16,19,20} a lack of this abnormality should not lead to a decrease in suspicion of this disease in cats without effusion, as only less than half (42.8%) of cats with non-effusive FIP in this study had elevated bilirubin levels.

An increase in total serum globulins, especially γ -globulins, is another commonly observed biochemical abnormality in cats with FIP thought to result mainly from non-specific immune responses.^{16,56–58} Past studies documented increased serum globulin levels in 39–66% of FIP cats.^{4,10,19} In the present study, hyperglobulinaemia was detected in 89.1% of cats (163/183) irrespective of effusion, indicating that this is a fairly sensitive albeit non-specific diagnostic test not only in cats with, but also without, effusion.

In previous studies, serum γ -globulin concentrations were found to have a high positive predictive value (PPV) for FIP.^{15,59} Determination of serum globulin fractions via protein electrophoresis was performed in only 47 cats in the present study, 48.9% (23/47) of which had a γ -globulin concentration $\geq 2.5 \text{ g/dl}$. This γ -globulin concentration was found to be the optimal cut-off value by Hartmann et al,¹⁵ with a specificity of 99%, a sensitivity of 35% and a PPV of 98%. The present study was performed in the same clinic as that of Hartmann et al,¹⁵ and drew cats from the same clinic population, only at a later time point, thus allowing the assumption that the cat

populations were very similar and enabling the application of the PPV calculated in that study. Based on the PPV of 98%, serum γ -globulins in the current study had a high diagnostic value in about half of the cats in which they were performed.

An increase in total protein, which is composed of the globulin fractions, as well as albumin, is often considered the most common laboratory abnormality in cats with FIP.^{16,56} However, while studies exist documenting a high prevalence of elevated serum protein levels in cats with FIP,^{4,19,60} other studies have reported hyperproteinaemia in a considerably lower percentage.^{10,19,20} Thus, Sparkes et al detected high total protein levels in only 39% of cats with FIP.¹⁹ Moreover, the current study documented hyperproteinaemia in only 17.5% (32/183) of cats. Similar to a study by Pedersen,⁶¹ an increase in total protein was significantly more common in cats without than with effusion. The most likely explanation for the low percentage of cats with hyperproteinaemia in the present study is the high prevalence of hypoalbuminaemia, observed in 64.5% of cats. The fact that hypoalbuminaemia and effusion caused by extravasation of protein-rich fluids are common findings in cats with FIP,^{16,47} leading to a decrease in total protein values, suggests that serum total protein is not a reliable diagnostic marker for FIP.

A:G ratio, the second serum parameter that takes globulins and albumin into account, presents a more valuable diagnostic tool than total protein levels.^{15,62,63} Serum A:G ratio decreases in cats with FIP because, as discussed above, globulin levels usually increase while albumin levels tend to decrease.^{4,15,63} Hypoalbuminaemia in cats with FIP is most commonly attributable to extravasation secondary to vasculitis in cats with effusion and, especially in cases of only slight decreases in albumin levels, to albumin's role as a negative acute phase protein.^{23,64} Thus, in the current study, 64.5% (118/183) of cats with FIP were hypoalbuminaemic, and decreased albumin levels were correlated to effusion. A:G ratio, in contrast, was not associated with effusion, indicating that globulin concentration is a weightier determinant of A:G ratio than the albumin level. Similar to Rohrer et al,⁴ 85% (155/183) of cats with FIP had an A:G ratio with an optimal cut-off value of <0.8 .^{15,63} In the study by Hartmann et al,¹⁵ a cut-off value <0.8 was associated with a specificity of 79%, a sensitivity of 87% and a PPV of 80%.¹⁵ While the selection of lower cut-off values increases the specificity and PPV of A:G ratio, it also decreases sensitivity.¹⁵ In the current study, 67.8% (124/183) of cats had an A:G ratio <0.6 , which had a specificity of 85%, a sensitivity of 67% and a PPV of 83%.¹⁵ Comparing the present study to that of Hartmann et al,¹⁵ the proportion of infected cats with a decreased A:G ratio was very similar for both cut-off values, which most likely reflects the similar study populations.

Conclusions

As previously established, young age and male sex were significantly correlated with FIP, while reproductive status of neither sex was associated with disease. Microcytosis with and without anaemia was common, suggesting that the presence of this laboratory abnormality in a cat with other clinical and laboratory parameters consistent with FIP can increase suspicion of this disease. Lymphopenia and hyperbilirubinaemia, both considered typical laboratory abnormalities in cats with FIP, were observed infrequently in cats without effusion. Over a third of cats with a left shift lacked a mature neutrophilia, a finding more expected in sepsis,^{50,51} which could potentially complicate the differentiation of effusive FIP from septic peritonitis, especially in cats without toxic change or those pretreated with antibiotics. Hyperproteinaemia, commonly considered a frequent finding in cats with FIP,^{15,56} was observed in only <20% of cats, indicating that serum total protein is not a reliable diagnostic parameter for FIP. Hyperglobulinaemia was detected in 89.1% of cats with FIP, suggesting that this is a fairly sensitive albeit non-specific diagnostic test in cats with and without effusion. While only measured in a relatively small number of cats, serum γ -globulins had a high diagnostic value (based on a PPV of 98%)¹⁵ in approximately half of the 47 cats on which it was performed. An A:G ratio <0.8, detected in 85% of cats with FIP, was also considered to be of diagnostic value based on the specificity and PPV determined by Hartmann et al.¹⁵

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