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A retrospective clinical and epidemiological study on feline coronavirus (FCoV) in cats in Istanbul, Turkey

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ABSTRACT

The presence of antibodies to feline coronavirus (FCoV) and feline immunodeficiency virus (FIV), together with feline leukemia virus (FeLV) antigen was investigated in 169 ill household and stray cats attending a veterinary surgery in Istanbul in 2009–14. The estimated FCoV and FIV seroprevalence (95% confidence intervals) were 37% (30–45%) and 11% (6–16%), respectively and FeLV prevalence was 1% (0–3%). FCoV seroprevalence increased until 2 years of age, was highest in 2014 and among household cats living with other cats and with outdoor access, and was lower in FIV seropositive compared to seronegative cats. Symptoms typically associated with wet feline infectious peritonitis (FIP) including ascites, abdominal distention or pleural effusion, coupled in many cases with non-antibiotic responsive fever, were observed in 19% (32/169) of cats, and 75% (24/32) of these cats were FCoV seropositive. FCoV seropositivity was also associated with a high white blood cell count, high plasma globulin, low plasma albumin and low blood urea nitrogen. The percentage of FCoV seropositive and seronegative cats that died in spite of supportive veterinary treatment was 33% (21/63) and 12% (13/106), respectively. These results indicate that FCoV is widespread and has a severe clinical impact in cats from Istanbul. Moreover, the incidence of FCoV infections could be rising, and in the absence of effective vaccination cat owners need to be made aware of ways to minimize the spread of this virus.

1. Introduction

Feline coronaviruses (FCoVs) are enveloped, positive-sense, single-stranded RNA viruses classified as "subgroup 1a" in the family *Coronaviridae* within the order *Nidovirales* (Vijaykrishna et al., 2007). FCoVs consist of two biotypes designated as feline enteric coronavirus (FECV) and feline infectious peritonitis virus (FIPV), which are both divided into two serotypes, I and II. Serotype I is of feline origin and difficult to grow in cell culture. Serotype II appears to have arisen from the recombination of FCoV serotype I with canine coronavirus and grows rapidly in cell culture causing a lytic cytopathic effect (Benetka et al., 2004; Hartmann, 2005;Pedersen, 2009). It is thought that the FIPV biotype may arise from FECVs in individual cats by internal mutation, often in immune suppressed cats (Poland et al., 1996; Vennema, 1999). An alternative hypothesis is that FECVs and FIPVs form distinct viral populations with infection by FIPV causing FIP (Brown et al., 2009).

FCoVs are transmitted by the fecal–oral route and the virus can persist on fomites for 3–7 weeks where they pose a risk of transmission (Hartmann, 2005; Pedersen, 2009;

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Kipar et al., 2010). FCoVs primarily infect enterocytes and spread from the intestine by monocyte-associated viremia (Gunn-Moore et al., 1998; Kipar et al., 2005). They have also been shown to replicate in monocytes/macrophages of healthy cats (Can-Sahna et al., 2007; Dye et al., 2008). Vertical transmission has not been demonstrated (Foley et al., 1997). Persistently infected, asymptomatic carriers spread FCoV since most of these cats shed the virus for a period of months or years, either continuously or transiently (Foley et al., 1997; Cave et al., 2004; Dye et al., 2008; Kipar et al., 2010; Sabshin et al., 2012).

The symptoms of FCoV infection are highly variable. Most FCoV-infected cats look healthy with the exception of a mild enteritis (Pedersen, 2009). Up to 12% of FCoV infected cats develop feline infectious peritonitis (FIP), which is a fatal form of the infection (Addie et al., 2009). Development of FIP is strongly associated with stress, immunity, multi-cat households and mainly occurs in young cats between 3 and 16 months of age (Cave et al., 2004; Hartmann, 2005; Bell et al., 2006; Addie et al., 2009; Vogel et al., 2010). Clinically, two forms of FIP are well documented: a 'wet' or effusive form (polyserositis and vasculitis) and a 'dry' or non-effusive form (pyogranulomatous lesions in organs) (Kipar et al., 2005). Ascites is the most prominent manifestation of 'wet form' FIP while lethargy, anorexia, weight loss and fever refractory to antibiotics are common and non-specific signs of FIP (Kipar et al., 2005; Addie et al., 2009).

Diagnosis of FIP is complicated and the cat's clinical history together with results from several analyses including serology, PCR and postmortem analyses are often required before a definite diagnosis can be reached (Shelly et al., 1988; Hartmann et al., 2003; Addie et al., 2004, 2009; Pratelli, 2008; Sharif et al., 2010; Taylor et al., 2010). Hematological and biochemical changes in FIP cases are not very specific, but ascites, increase in serum protein level, increase in bilirubin, decrease in hematocrit and decrease in A:G ratio are prominent (Addie et al., 2009). Serological tests may fail to detect recent infections and cross-reactions occur between FIPV and low pathogenic FECV strains (Hartmann, 2005, Sharif et al., 2010). Molecular detection systems like standard and real time reverse transcription polymerase chain reaction (PCR) have certain advantages as they are rapid and sensitive, particularly when using abdominal or pleural fluidor tissue biopsy or aspirates (Pedersen, 2009; Sharif et al., 2010). A recent PCR test that is commercially available (FIP Virus RealPCR™ Test, IDEXX) allows differentiating FIPV and low pathogenic FECV biotypes, and according to the manufacturers, the test was 99.4% accurate in samples from 88% infected cats with a positive PCR result. PCR results should be evaluated together with clinical findings and postmortem samples should be analyzed by molecular methods (Sparkes et al., 1994; Hartmann et al., 2003; Pratelli, 2008; Addie et al., 2009; Pedersen, 2009; Sharif et al., 2010).

Worldwide the prevalence of FCoV infections may be up to 90% in multi-cat environments and 10–60% in household cats (Herrewegh et al., 1997; Pedersen et al., 2004; Bell et al., 2006; Addie et al., 2009; Sharif et al., 2009; Taharaguchi et al., 2012). Detection of FCoV antibodies in the early stage of infection can be useful to minimize the spread of FCoVs in a breeding cattery, multi-cat household and FCoV-free household (Cave et al., 2004; Dye et al., 2008; Drechsler et al., 2011). Therefore, it is important to monitor cats living in multi-cat environments in order to reduce and control FCoV infection.

The aim of this study was to investigate FCoV seroprevalence and its relationship with the animal's signalment, habitat, hematological and biochemical parameters and symptoms in cats from Istanbul.

2. Materials and methods

2.1. Study population and sampling

During 5 years, from January 2009 to April 2014, a total of 169 cats with symptoms compatible with feline viral infections were included in the study population. They included individuals with fever, depression, dullness and/or weight loss. They were examined by two different veterinarians working at a private Veterinary Clinic in Istanbul. The animals' gender, breed, age and hábitat whether household, shelter or street (stray cats) was recorded. Other data from household cats included if they were adopted or home raised from birth, they cohabitated with other cats and had outdoor access.

Cats were clinically examined to detect fever, skin lesions, behavioral changes (insidious onset, depression) and symptoms related to organ systems were recorded; specifically, cardiorespiratory (dyspnea, abnormal heart and lung sounds), gastrointestinal (anorexia, weight loss, stomatitis, enteritis, abdominal distension, vomication, ascites), urinary, circulatory (lymphoadenopathy, anemia, icterus), ocular lesions (keratic precipitates, uveitis, hyphema, iridocyclitis, chorioretinitis) and central nervous system (epileptic seizures, ataxia) symptoms.

Blood samples were taken from the cephalic vein by the veterinarians examining the cats for hematological and biochemical analyses and to detect antibodies against FCoV and feline immunodeficiency virus (FIV) together with feline leukemia virus (FeLV) antigen as described below. All analysis except FCoV IFAT antibodies were carried out at the veterinary clinic within an hour of taking the blood sample. IFAT tests and protein electrophoresis were carried out at an external private veterinary laboratory.

Disease progression of the study cats was evaluated during repeat visits to the clinic and mortality was considered to be associated to the current infection when the cat did not respond to standard treatments which included fluid and antibiotic therapy.

2.2. Analysis of serum samples for antibodies to FCoV and FIV and for FeLV antigen

All serum samples ($n = 169$) were analyzed by rapid tests for the presence of antibodies to FCoV (Bionote, Anigen, FCoV) and FIV (Bionote, Anigen FIV Ab), and FeLV antigen (Bionote, FeLV Ag) following kits' instructions. According to the manufacturers, the sensitivity (Se) and specificity (Sp) of the FCoV test compared to the reference immunofluorescence antibody test (IFA) were 96.0% and 97.9%, respectively, Se and SP of the FeLV test versus virus