

The emerging landscape of feline coronavirus type II in Asia: a review of molecular diversity and diagnostic challenges

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Abstract. Feline infectious peritonitis (FIP) is a fatal systemic disease of cats caused by feline coronavirus (FCoV). FCoV is classified into two biotypes: feline enteric coronavirus (FECV) and feline infectious peritonitis virus (FIPV). In addition, FCoV comprises two serotypes, type I and type II, which are distinguished based on antigenic and genetic differences in the spike (S) protein. Globally, type I is more prevalent than type II. Despite the lower prevalence of type II, its distinct molecular characteristics, including recombination breakpoints within the S gene and variations in accessory genes such as 3c, indicate differences in viral evolution, cellular entry mechanisms, and replication efficiency. This review aims to summarize current knowledge on the molecular characteristics, epidemiology, pathogenesis, and diagnostic aspects of FIP type I and type II, with particular emphasis on data from Asian countries. The findings indicate that type I is the predominant serotype in Asia, whereas type II is detected at considerably lower frequencies.

1. Introduction

Feline infectious peritonitis (FIP) was first described as a distinct clinical entity in 1963 by Dr. Jean Holzworth in Boston, USA [1]. The disease is caused by feline coronavirus (FCoV) [2]. FCoV is a nonsegmented, single-stranded RNA virus classified within the order *Nidovirales*, family *Coronaviridae*, subfamily *Coronavirinae*, and genus *Alphacoronavirus 1* [3]. The virus is large, enveloped, and spherical, with prominent spike (S) glycoproteins projecting from its surface, giving it a characteristic crown-like appearance under electron microscopy [4].

Based on pathogenicity, FCoV is divided into two biotypes: feline enteric coronavirus (FECV), which is generally avirulent and commonly detected, and feline infectious peritonitis virus (FIPV), which is highly virulent [5]. These biotypes differ markedly in clinical outcome. FECV infection is typically asymptomatic and establishes persistent replication in the intestinal epithelium [6]. In contrast, FIPV represents a virulent variant that can lead to fatal systemic disease in cats. This shift in virulence is associated with a change

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in tissue tropism, from replication in the apical villi of the small intestine to infection of monocytes and macrophages [7].

The alteration in tissue tropism is thought to result from mutations within the FECV genome and amino acid substitutions in encoded viral proteins, although the exact mechanisms remain incompletely defined [7,8]. Two spike protein substitutions, M1058L and S1060A, have been associated with altered virulence and the transition from FECV to FIPV [9]. Both FECV and FIPV are further classified into type I and type II based on genetic and antigenic differences [10]. Type II viruses arise from recombination events between FCoV type I and canine coronavirus (CCoV) [11]. Globally, type I predominates over type II; however, type II has been reported with relatively higher frequency in certain Asian countries [12]. Therefore, this review aims to evaluate the prevalence and distribution of FCoV type II in Asia.

2. Result and discussion

3.1. Pathogenesis

Feline coronavirus (FCoV) is classified into two serotypes, FCoV type I and FCoV type II, based on differences in the amino acid sequence of the spike (S) protein [13]. Distinct receptor usage has been described between the two serotypes. The cellular receptor for FCoV type I remains unidentified, largely because this serotype does not readily adapt to cell culture systems, limiting *in vitro* characterization [14–15]. In contrast, FCoV type II adapts efficiently to cell culture, enabling the identification of its receptor as feline aminopeptidase N (fAPN) [4]. Although FCoV type II has been suggested to exhibit higher apparent virulence, it cannot be clearly distinguished into low-pathogenic FECV and high-pathogenic FIPV solely based on serotype classification [15]. Coinfection is uncommon; however, chronic feline immunodeficiency virus (FIV) infection may induce immunosuppression, thereby promoting enhanced intestinal replication of FECV and facilitating the emergence and selection of FIPV mutants by impairing the host's antiviral immune response [15].

The transition from FECV to FIPV depends largely on the infected cat's immune response. The clinical manifestation of FIP reflects the balance between humoral and cell-mediated immunity. The effusive form of FIP is associated with inadequate cell-mediated immunity, leading to dysregulated cytokine production and the development of body cavity effusions. In contrast, the non-effusive form occurs when partial cell-mediated immunity remains functional, allowing localization of the virus within specific tissues but failing to eliminate it completely [14]. FCoV initially replicates in the intestinal epithelium and may subsequently acquire mutations that enable replication in monocytes and macrophages [7]. Viral replication in intestinal epithelial cells, monocytes, or macrophages is associated with a high mutation rate, further driving viral evolution [4].

FECV mutates into FIPV during *in vivo* infection, enabling the virus to infect circulating monocytes and tissue macrophages. Mutations in accessory genes, particularly 3c and 7b, have been implicated in the development of FIP. The spike protein plays a central role in receptor binding via its S1 subunit and in membrane fusion via its S2 subunit [2]. Two spike protein amino acid substitutions, M1058L and S1060A, have been associated with increased virulence and the transition from FECV to FIPV [7,9]. These substitutions are considered potential molecular markers of FIPV, as they correlate with the virus's ability to infect and replicate within monocytes and macrophages, thereby supporting systemic dissemination.

The S gene is also widely used for molecular typing of FCoV. In FCoV type I, the S gene corresponds to the original feline spike sequence, whereas in FCoV type II, the S gene is derived from canine coronavirus (CCoV) as a result of recombination events. Because the

S gene encodes the spike protein, which represents the most variable region of the viral genome, it serves as a critical target for genetic characterization and strain differentiation [9].

3.2. Diagnosis

The nonspecific clinical manifestations of FIP make its diagnosis particularly challenging. A definitive diagnosis cannot be established based on a single diagnostic test, and the interpretation of laboratory results must always be integrated with the individual cat's clinical condition [5]. Currently, the most definitive diagnostic method for FIP is immunohistochemistry (IHC), which detects viral antigen in macrophages within characteristic inflammatory lesions [1, 15]. Samples suitable for diagnostic evaluation include blood, tissue biopsies, fine-needle aspirates (FNA), cerebrospinal fluid (CSF), and aqueous humor [15].

Reverse transcription polymerase chain reaction (RT-PCR) can detect FCoV RNA; however, this method is not specific for FIP, as FCoV RNA may also be detected in cases of FECV infection [19]. Quantitative RT-PCR (RT-qPCR) provides additional diagnostic value, as cats with FIP and compatible clinical findings typically exhibit higher viral loads compared to healthy carriers [5]. According to Thayer et al. (2022) [1], RT-qPCR represents one of the most reliable approaches for quantifying FCoV RNA in clinical samples, offering greater diagnostic confidence than simple detection of viral presence alone.

Molecular typing of FCoV into types I and II can be performed using sequencing or mutation-specific PCR assays [5, 11]. Sequence analysis commonly focuses on the S gene, particularly the S2 fusion domain region in type I FCoV. Specific spike protein mutations, including M1058L and S1060A, have been identified in tissues from cats with FIP but are not typically detected in clinically healthy cats [15]. These mutations are therefore considered useful molecular markers associated with systemic infection and FIP pathogenesis.

3.3. Prevalence and Epidemiology in Asia

FIP is classified into two serotypes, FCoV type I and type II. The primary difference between these serotypes lies in the spike (S) protein, which induces virus-neutralizing (VN) antibodies and serves as the basis for serological differentiation [10]. A review of the literature on the prevalence and molecular identification of FIP in Asia consistently demonstrates that type I is markedly more dominant than type II. According to several reports, approximately 80–90% of cats with confirmed FIP are infected with FCoV type I.

Table 2. Prevalence and Epidemiology of FIP in Asia

Author	Country	Type I Prevalence (%)	Type II Prevalence (%)	Detection Method
Lin et al (2021)	China	98.72% (77/78)	1.28% (1/78)	PCR
Shiba et al (2007)	Japan	98% (49/50)	2% (1/50)	VN test
Kim et al (2025)	South Korea	90.9% (20/22)	9.1% (2/22)	RT-PCR
Amer et al (2012)	Malaysia	98% (39/40)	2% (1/40)	RT-PCR
Yen et al (2021)	Taiwan North	71.9% (23/32)	28.1% (9/32)	RT-PCR
Techangamsuwan et al (2012)	Thailand	47.45% (28/59)	17% (10/59)	RT-PCR

Based on the reviewed studies, the highest reported proportion of type II was observed in Taiwan, where it accounted for 28.1% (9/32) of cases. In other countries, including China, Japan, South Korea, and Thailand, only one to two cats were identified as infected with FCoV type II. In the literature analyzed, FCoV type II was detected exclusively in FIP samples. This finding is consistent with a previous study, which reported that FCoV type II was

identified only in cats diagnosed with FIP, not in clinically healthy cats. However, Kim et al. (2025) [12] emphasized that these data do not definitively establish a direct association between type II infection and FIP development. Furthermore, a study conducted in China demonstrated that overall FCoV prevalence was not significantly associated with gender, geographical location, breed, or viral coinfection, but was significantly associated with age [11].

Several biological factors may contribute to the lower prevalence of FCoV type II. Previous research has suggested that type II exhibits reduced replication efficiency *in vivo*, resulting in lower viral loads and antibody titers than type I. This reduced replication capacity may partly explain the lower detection rates of type II in field studies. In contrast, FCoV type I appears to be better adapted to feline hosts, whereas type II originates from recombination events between feline and canine coronaviruses, which may influence its evolutionary fitness in cats.

Despite its lower prevalence, FCoV type II has been reported to spread horizontally among cats sharing the same environment. The potential for horizontal transmission, particularly in multi-cat settings, raises epidemiological concerns and highlights the importance of accurate serotyping and molecular identification of FIP cases to better understand transmission dynamics and implement appropriate control strategies.

3. Conclusion

This review demonstrates that FCoV type I remains the predominant serotype circulating in Asian cat populations, whereas type II is detected at significantly lower frequencies. The epidemiological dominance of type I likely reflects its stronger adaptation to feline hosts and its stable transmission within multi-cat environments. In contrast, type II arises from recombination events between feline and canine coronaviruses and appears to circulate less efficiently in natural field conditions despite its ability to replicate more readily *in vitro*.

Current evidence does not conclusively indicate that type II is inherently more pathogenic than type I. Both serotypes can cause either low-pathogenic FECV or highly pathogenic FIPV, and disease progression is primarily determined by viral mutations, particularly in the spike gene and in accessory genes such as 3c, as well as by the host immune response. Although type II has been detected almost exclusively in FIP cases in several studies, its low prevalence and reduced viral load may contribute to underdetection and limited epidemiological impact.

Molecular typing, particularly targeting the S gene, is essential for accurate epidemiological surveillance and for understanding viral evolution, recombination dynamics, and transmission patterns in Asia. Given the potential for horizontal transmission and interspecies recombination, continuous monitoring of circulating FCoV strains is necessary. A clearer understanding of the molecular and epidemiological characteristics of FCoV type I and II will improve diagnostic interpretation, support targeted control strategies, and provide a stronger foundation for future therapeutic and preventive approaches.

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