

Geographic Distribution, Prevalence and Diagnostic Methods of Domestic Cat Hepadnavirus (DCH): A Scoping Review

(DISTRIBUSI GEOGRAFIS, PREVALENSI, DAN METODE DIAGNOSTIK
DOMESTIC CAT HEPADNAVIRUS (DCH): SCOPING REVIEW)

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ABSTRACT

Domestic cat hepadnavirus (DCH) is a virus first identified in 2018 and classified within the family *Hepadnaviridae*. This study aimed to summarize the geographical distribution, reported prevalence, and diagnostic methods of DCH infection through a scoping review of the available literature. A systematic literature search was conducted in PubMed, ScienceDirect, Scopus, and Google Scholar to identify English-language primary research articles published between 2018 and 2025, following the PRISMA-ScR guidelines. Studies meeting the inclusion criteria were selected based on predefined criteria and analyzed descriptively by extracting information on study location, sample size, detection methods, and reported prevalence estimates. A total of 26 articles met the inclusion criteria and were included in this review. The findings indicate that DCH has been reported in multiple countries across Asia, Europe, the Americas, and Oceania, with most publications originating from Southeast Asia and Europe. Reported prevalence varied widely, ranging from 0.2% to 17.6%, which may be influenced by differences in study design, population characteristics, geographic settings, sampling strategies, and specimen types. Molecular diagnostic approaches, particularly polymerase chain reaction (PCR) and quantitative

polymerase chain reaction (qPCR), were the most commonly used methods, primarily applied to blood or serum samples, while serological and histopathological approaches were reported less frequently. Overall, the available epidemiological evidence remains heterogeneous and influenced by methodological variability across studies. Therefore, standardization of study design and diagnostic protocols is required to generate more consistent and globally comparable estimates of DCH distribution and prevalence.

Keywords: domestic cat hepadnavirus; geographic distribution; prevalence; diagnostic methods; scoping review.

ABSTRAK

Domestic cat hepadnavirus (DCH) merupakan virus yang pertama kali diidentifikasi pada tahun 2018 dan termasuk dalam famili *Hepadnaviridae*, dengan kemiripan genetik yang tinggi terhadap virus hepatitis B pada manusia. Penelitian ini bertujuan merangkum distribusi geografis, prevalensi yang dilaporkan, serta metode diagnostik infeksi DCH melalui *scoping review* terhadap literatur yang tersedia. Pencarian literatur sistematis dilakukan pada basis data PubMed, ScienceDirect, Scopus, dan Google Scholar untuk mengidentifikasi artikel penelitian primer berbahasa Inggris yang dipublikasikan antara tahun 2018 hingga 2025, mengikuti pedoman PRISMA-ScR. Studi yang memenuhi kriteria inklusi diseleksi menggunakan kriteria yang telah ditetapkan dan dianalisis secara deskriptif dengan mengekstraksi informasi mengenai lokasi penelitian, ukuran sampel, metode deteksi, serta estimasi prevalensi yang dilaporkan. Sebanyak 26 artikel memenuhi kriteria inklusi dan dianalisis dalam penelitian ini. Hasil telaah menunjukkan bahwa DCH telah dilaporkan di berbagai negara di Asia, Eropa, Amerika, dan Oseania, dengan sebagian besar publikasi berasal dari Asia Tenggara dan Eropa. Prevalensi yang dilaporkan bervariasi cukup luas, berkisar antara 0,2% hingga 17,6%, yang kemungkinan dipengaruhi oleh perbedaan desain penelitian, karakteristik populasi, lokasi geografis, strategi pengambilan sampel, dan jenis spesimen yang digunakan. Pendekatan diagnostik molekuler, khususnya *polymerase chain reaction* (PCR) dan *quantitative polymerase chain reaction* (qPCR), merupakan metode yang paling umum digunakan, menggunakan sampel darah atau serum, sedangkan metode serologis dan histopatologis dilaporkan lebih terbatas. Secara keseluruhan, data epidemiologis DCH masih heterogen dan dipengaruhi variasi metodologis, sehingga diperlukan standarisasi desain penelitian dan protokol diagnostik untuk menghasilkan estimasi distribusi dan prevalensi yang lebih konsisten serta dapat dibandingkan secara global.

Kata-kata kunci: *domestic cat hepadnavirus*; distribusi geografis; prevalensi; metode diagnostik; *scoping review*

INTRODUCTION

Hepadnaviruses are a family of partially double-stranded DNA viruses that infect a wide range of mammalian and avian species (Dill *et al.*, 2016). The most clinically significant member is human hepatitis B virus (HBV), which remains a major global public health problem. It is estimated

that 296 million people live with chronic HBV infection worldwide, resulting in approximately 820,000 deaths annually due to cirrhosis and hepatocellular carcinoma (HCC) (Razavi *et al.*, 2018). Beyond humans, hepadnaviruses have been identified in several animal species, including woodchucks and equids, highlighting their broad host range and evolutionary adaptability (Daffis *et al.*, 2021; Rasche *et al.*, 2021).

Domestic cat hepadnavirus (DCH) was first identified in 2018 in immune-compromised domestic cats in Australia and was classified within the family *Hepadnaviridae*, genus *Orthohepadnavirus* (Aghazadeh *et al.*, 2018). Phylogenetic analyses demonstrate a close genetic relationship between DCH and HBV, with conserved genomic regions such as epsilon (ϵ) and direct repeat (DR) elements that indicate similar replication strategies (Capozza *et al.*, 2023). The DCH genome consists of a partially double-stranded circular DNA molecule of approximately 3,184-3,187 base pairs. Since its discovery, DCH has been reported in Australia, Asia, Europe and the Americas, with prevalence varying widely across regions and study populations (Shofa *et al.*, 2022).

Experimental studies have shown that DCH utilizes the same cellular entry receptor as HBV, namely the sodium taurocholate cotransporting polypeptide (NTCP) and that DCH can enter human-derived hepatocyte cell lines *in vitro* (Shofa *et al.*, 2023). However, there is currently no clinical or epidemiological evidence of natural DCH infection in humans or cross-species transmission between cats and humans. Accordingly, DCH is not classified as a zoonotic disease at present. Nonetheless, its phylogenetic relatedness to HBV and shared receptor usage highlight the importance of continued investigation within a One Health framework.

Several studies have reported associations between DCH infection and chronic hepatitis, elevated alanine aminotransferase (ALT) activity, hepatocellular carcinoma (HCC) and lymphoma in cats. However, most available evidence derives from cross-sectional or retrospective studies and causal relationships have not yet been conclusively established. Co-infection with feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV) has also been frequently documented, suggesting that immunocompromised states may facilitate viral persistence. Diagnostic approaches include molecular de-

tection using polymerase chain reaction (PCR) and quantitative polymerase chain reaction (qPCR) to identify active viremia, as well as serological assays to detect antibody responses (Pesavento *et al.*, 2019; Anpu-anandam *et al.*, 2021; Piewbang *et al.*, 2022; Piewbang *et al.*, 2023; Cavasin *et al.*, 2025). Differences in diagnostic methods may partly explain variations in reported prevalence and clinical associations across studies.

Although DCH has been reported in several Southeast Asian countries, including Thailand, Malaysia, Hong Kong and Taiwan, it has not yet been formally documented in Indonesia (Shofa *et al.*, 2022). Indonesia has a large population of owned and stray cats, which may facilitate virus maintenance and transmission. To address the current lack of local data and enhance clinical awareness among local practitioners, this study was aimed to systematically map and synthesize global scientific evidence regarding the geographic distribution, prevalence and diagnostic methods of DCH. This synthesis provides crucial insights into the epidemiological implications and surveillance strategies for emerging infectious diseases affecting Indonesia's domestic cat populations.

RESEARCH METHODS

A scoping review methodology was employed for this study. This approach was selected given the recent identification of DCH and the limited body of available literature. This framework is specifically designed to identify and map the breadth of evidence in an emerging field, providing a foundational synthesis of available data to guide future research priorities.

The preparation and reporting of this review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR), which includes 17 items in a reporting checklist specifically designed

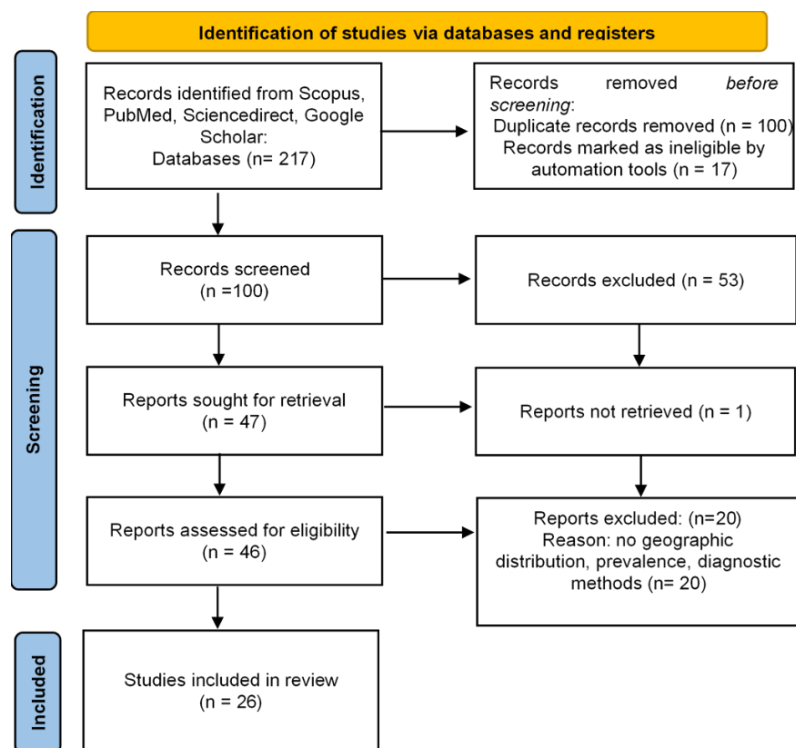


Figure 1. Study selection flow diagram based on PRISMA-ScR guidelines. The diagram shows the stages of identification, screening, feasibility assessment, and inclusion of articles in domestic cat hepadnavirus (DCH) scoping review (Tricco *et al.*, 2018). The number n indicates the number of articles at each stage of selection. Articles are excluded at the full-text assessment stage if they do not report geographic distribution, prevalence or frequency of detection, and DCH diagnostic methods (Peters *et al.*, 2020).

for scoping reviews (Tricco *et al.*, 2018). The study selection process is presented in Figure 1 according to the PRISMA-ScR flow diagram. Literature searches were conducted systematically in PubMed, Scopus, ScienceDirect and Google Scholar using combinations of English-language keywords related to domestic cat hepadnavirus, geographic distribution, prevalence and diagnostic methods. The search was restricted to English-language primary research articles published from 2018 to December 2025.

All retrieved records were compiled and deduplicated using Mendeley software and then screened by title and abstract using the Rayyan platform according to predefined inclusion and exclusion criteria. Inclusion criteria comprised primary studies that investigated DCH in domestic cats and reported geographic distribution, prevalence or

detection frequency, and/or diagnostic methods (Peters *et al.*, 2020). Articles were excluded if they involved non-Felidae species, focused on hepadnaviruses other than DCH, were review articles, or did not present relevant primary research data. Articles that passed the initial screening were assessed for eligibility through full-text review and all reasons for exclusion at this stage were documented according to PRISMA-ScR guidelines.

Data from studies that met the inclusion criteria were extracted and synthesized descriptively to map the geographic distribution, prevalence ranges or detection frequencies and the diversity of DCH diagnostic methods. Studies with retrospective or case-based designs were included to provide

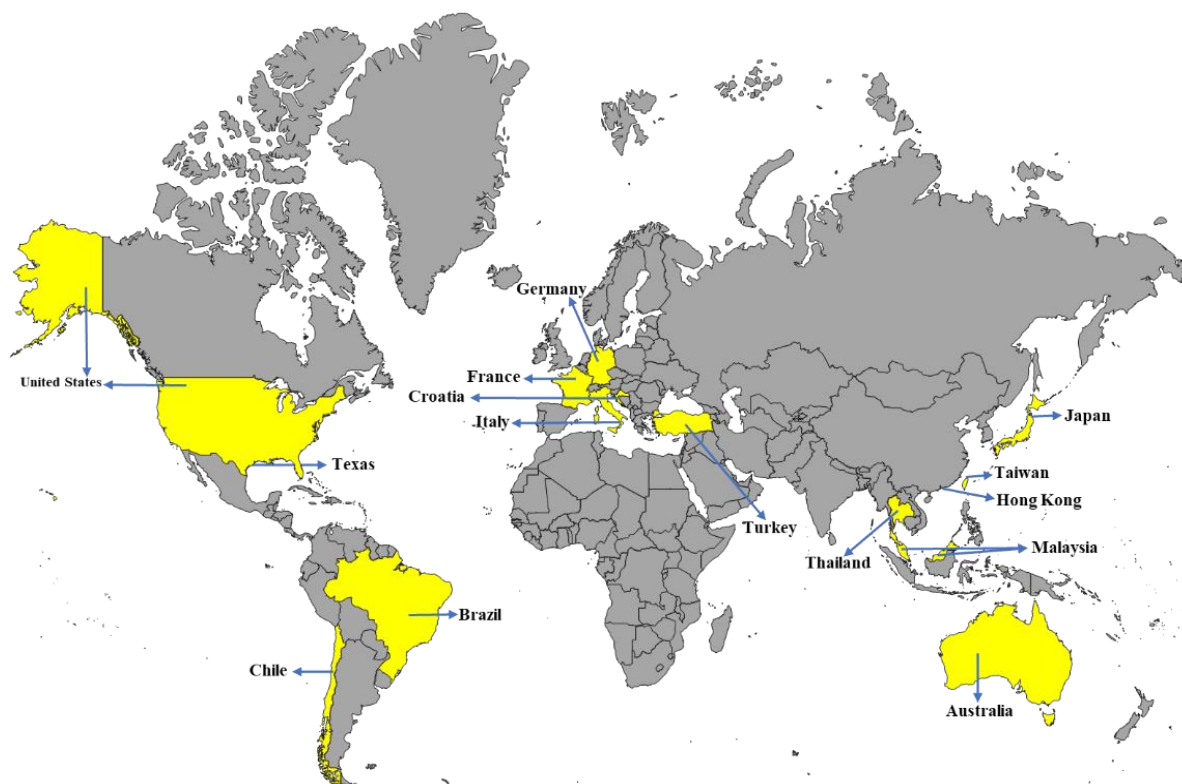


Figure 2. Geographical distribution map of countries reporting domestic cat hepatitis virus (DCH) studies adapted from Shofa *et al.* (2022). Countries highlighted in yellow represent locations with published DCH research, whereas grey-colored countries indicate no reported studies based on the included articles.

an overview of the spectrum of available diagnostic and clinical evidence, but were not used as the basis for estimating population-level prevalence.

RESULTS AND DISCUSSION

A systematic literature search identified several articles relevant to DCH. The processes of study identification, screening and selection were conducted in accordance with the PRISMA-ScR guidelines and are summarized in the PRISMA flow diagram (Figure 1) (Tricco *et al.*, 2018). Following the application of predefined inclusion and exclusion criteria, a total of 26 studies were included in this scoping review and subjected to further analysis.

Mapping of the geographical distribution is presented in Figure 2. reveals that

DCH has been reported in multiple countries, with the predominance of published reports originating from Southeast Asia and Europe, particularly from Japan and Malaysia (Anpu-anandam *et al.*, 2021). This geographic pattern, however, appears to reflect substantial publication bias and research intensity disparities rather than the true epidemiologic distribution of the virus (Shofa *et al.*, 2022).

The concentration of DCH reports in specific regions likely reflects a combination of interconnected factors, established molecular diagnostic capacity, better access to research infrastructure and funding, active research networks and larger domestic cat populations, including both pet and stray cats (Stone *et al.*, 2022; Chen *et al.*, 2025).

In contrast, the apparent absence of identified DCH reports from many regions, including most of Africa, parts of Southeast Asia (notably Singapore), and Central/South

America, should not be interpreted as definitive evidence of non-circulation. Rather, this pattern more likely reflects limited surveillance and reduced publication representation in indexed databases. These disparities suggest that DCH may be more geographically

widespread than currently documented, underscoring the need for expanded surveillance and standardized diagnostic approaches to improve global epidemiologic comparability.

Tabel 1. Prevalence of domestic cat hepadnavirus (DCH) based on blood specimens with cross-sectional studies

Country	Author (Year)	Study design	Specimen types	DCH posi-tive/ total sample (n)	Prevalence DCH (%)
Australia	(Aghazadeh <i>et al.</i> , 2018)	Cross- Sectional	Blood	6/60	10.0%
				2/63	3.2%
Malaysia	(Stone <i>et al.</i> , 2022)	Cross- Sectional	Blood	7/67	10.4%
				31/253	12.3%
Thailand	(Piewbang <i>et al.</i> , 2022)	Cross- Sectional	Serum	26/209	12.4%
				25/532	4.70%
Japan	(Takahashi <i>et al.</i> , 2022)	Cross- Sectional	Blood	1/139	0.78%
				2/203	0.98%
Hong Kong	(Beatty <i>et al.</i> , 2024)	Cross- Sectional	Blood	34/193	17.6%
				57/513	11.1%
Taiwan	(Silva <i>et al.</i> , 2023)	Cross- Sectional	Blood	8/71	11.27%
Turkey	(Adıgüzel) <i>et al.</i> , 2023)	Cross- Sectional	Blood	17/498	3.41%
Italy	(Lanave <i>et al.</i> , 2019)	Cross- Sectional	Serum	42/390	10.8%
Chile	(Choi <i>et al.</i> , 2024)	Cross- Sectional	Blood	2/120	1.67%
Brazil	(Tessmann <i>et al.</i> , 2024)	Cross- Sectional	Serum	3/60	1.67%
				2/1.065	0.2%
United States	(Stone <i>et al.</i> , 2022)	Cross- Sectional	Blood	1/496	0.2%
				3/400	0.8%
European Countries	(Oliveira-filho <i>et al.</i> , 2025)	Cross- Sectional	Serum	7/1.195	0.6%

Note: Data in this table were synthesized from cross-sectional studies evaluating the presence of DCH using blood or serum specimens. Prevalence is reported as the proportion of positive samples

Table 2. Prevalence of domestic cat hepadnavirus (DCH) in longitudinal, case-control, and retrospective studies

Country	Author (Year)	Study design	Specimen types	DCH positive/ total sample (n)	PrevalenceDCH (%)
Thailand	(Wardhani <i>et al.</i> , 2025)	Observational longitudinal	Blood	4/87;	4.6%;
	(Piewbang <i>et al.</i> , 2023)	Case-control	Blood (Lymphoma cats)	11/68	16.18%
			Blood (Non-lymphoma cats)	19/526	3.51%
Italy	(Ratti <i>et al.</i> , 2023)	Retrospective	Serum (Effusion)	2/33	6.1%
			Serum (without effusion)	0/39	0

Note: This table summarizes studies with designs other than cross-sectional, including longitudinal observational, case-control, and retrospective studies, that reported DCH detection using blood or serum specimens. Prevalence is presented on a specimen-specific basis (n/N) according to the clinical groups reported in each study. Retrospective studies using non-blood specimens (e.g., tissue or effusion fluids) were not included in this table, as differences in specimen types may affect prevalence estimates.

While current evidence does not demonstrate natural zoonotic transmission of DCH to humans, several molecular and phylogenetic features warrant continued vigilance from a One Health perspective. The DCH shares the same NTCP receptor with hepatitis B virus, demonstrates *in vitro* capacity to infect human hepatocytes, and exhibits high phylogenetic relatedness to HBV, suggesting potential compatibility with human hosts despite the absence of epidemiological evidence of natural infection (Shofa *et al.*, 2023; Choonnasard *et al.*, 2024; Wardhani *et al.*, 2025; Shofa *et al.*, 2025).

A One Health framework is therefore essential, requiring integrated surveillance of DCH in domestic cat populations and epidemiological monitoring of at-risk human populations (veterinarian, cat breeders/lovers, shelter workers). Continued research into DCH host range, pathogenicity mechanisms, and genetic variability, coupled with its value

as an experimental model for HBV studies, will clarify the biological and epidemiological implications of this virus while strengthening scientific preparedness strategies. Prevalence summaries are presented based on the study design to facilitate the interpretation of DCH data. Studies with cross-sectional and non-cross-sectional designs are shown separately in Table 1 and Table 2.

Table 1 presents the most notable variation in DCH prevalence across cross-sectional studies, which serve as the primary basis for population-level prevalence estimates. Differences in prevalence estimates between studies are influenced by the characteristics of the sampled populations, including cat health status, clinical versus community settings, husbandry conditions and differences in inclusion criteria and diagnostic protocols. Cross-sectional studies provide a snapshot of prevalence at a single point in time and are generally more repre-

sentative for describing infection distribution at the population level than other designs. Table 2 summarizes studies with non-cross-sectional designs, including retrospective,

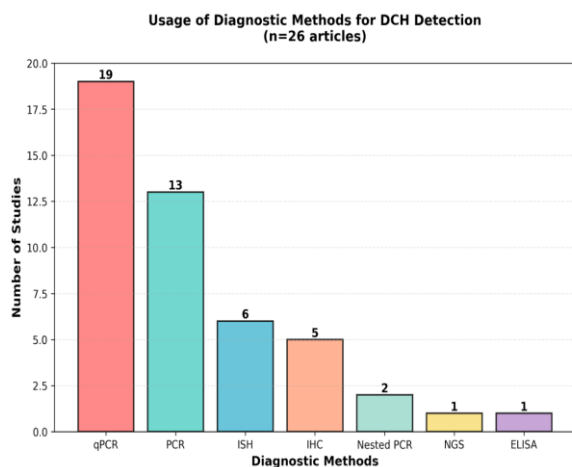


Figure 3. Distribution of diagnostic methods used in domestic cat hepatitis virus (DCH) studies included in the scoping review during the 2018–2025 period (n = 26). The reported diagnostic methods include polymerase chain reaction (PCR), quantitative PCR (qPCR), in situ hybridization (ISH), immunohistochemistry (IHC), nested PCR, and enzyme-linked immunosorbent assay (ELISA).

longitudinal and case-based investigations, which involve more diverse populations and clinical contexts. These studies add information on DCH detection patterns in cats with specific clinical conditions, such as chronic liver disease and impaired immune status and describe the dynamics of viral detection beyond the context of population surveys. The variation in study design underscores the importance of considering diagnostic approaches and sampling strategies when interpreting DCH detection results. The range and frequency of diagnostic approaches utilized in the included studies are summarized in Figure 3. This overview provides a general representation of the methodological strategies adopted for the detection and investigation of DCH within the scope of this review.

Consistent with the distribution of diagnostic methods shown in Figure 3, molecular techniques, particularly PCR and

qPCR, were the predominant approaches used in the included studies. These assays have high analytical sensitivity. Some studies have demonstrated that DCH testing protocols can be performed without prior nucleic acid extraction, thereby simplifying laboratory workflows and reducing analysis time and costs (Shofa *et al.*, 2023). In this review, the focus on prevalence data derived from blood or serum specimens was adopted as a methodological strategy to improve comparability between studies. The presence of DCH in the bloodstream reflects viremia and systemic infection status, allowing more consistent comparison of results across studies with different designs and populations (Anpuanandam *et al.*, 2021; Sakamoto *et al.*, 2023). However, the use of blood-based specimens is not the only approach reported, and several studies have also evaluated other biological matrices.

Some studies have reported DCH detection in non-blood specimens, including organ tissues, pleural effusion, urine and oral or nasal swabs, providing insights into tissue tropism and potential viral shedding routes. However, detection in these specimens more likely reflects local viral replication and shedding, which are influenced by tissue distribution, stage of infection, and variability in sampling techniques, potentially resulting in heterogeneous detection rates between studies (Wardhani *et al.*, 2023; Pesavento *et al.*, 2019; Adgzel *et al.*, 2023; Ratti *et al.*, 2023; Cavašin *et al.*, 2025). These differences become particularly relevant when DCH detection results are interpreted in relation to specific clinical conditions and the overall health status of affected cats.

Several studies have reported co-infection of DCH with FIV and FeLV, with particularly high frequency of co-detection with FIV, as well as detection of DCH in cats with chronic liver disease, including HCC and lymphoma (Piewbang *et al.*, 2020; Cavašin *et al.*, 2025). Significantly elevated proviral DNA loads were observed in FeLV and DCH co-infected cats compared to DCH mono-infected individuals, suggesting increased viral replication or persistence in immunocompromised states. These findings

have important clinical implications, The DCH should be considered in cats presenting with chronic liver-related abnormalities, such as elevated liver enzymes, jaundice, or weight loss, particularly in those co-infected with FIV or FeLV (Piewbang *et al.*, 2020; Shofa *et al.*, 2022).

Beyond domestic cats, DCH infection has also been reported in Iberian lynxes (*Lynx pardinus*) (Diakoudi *et al.*, 2025), suggesting potential circulation across the domestic–wildlife interface. Although the clinical and ecological impact of DCH in wild populations remains uncertain, such findings highlight the importance of integrated surveillance strategies that encompass both domestic and wild felid populations. Preventive considerations may include promoting responsible cat ownership, ethical management of stray cat populations, and targeted molecular monitoring within shared ecological zones. Future research employing prospective longitudinal designs and standardized diagnostic protocols will be essential to clarify transmission dynamics, host range, ecological implications and the broader epidemiologic and conservation significance of DCH.

CONCLUSION

This scoping review demonstrates that DCH virus has been detected across diverse geographical regions, with prevalence ranging from 0.2% to 17.6% and varying considerably according to study design, population characteristics, diagnostic methods and specimen types. Cross-sectional studies provide the primary basis for describing DCH prevalence at the population level, while non-cross-sectional studies contribute to a broader understanding of viral detection patterns within specific clinical contexts, including associations with chronic liver disease and co-infections with FIV or FeLV. Molecular PCR-based diagnostic methods, particularly qPCR, using blood or serum specimens represent the most consistent and analytically sensitive approach across stu-

dies, whereas findings from non-blood specimens and from cats with co-infections or chronic liver disease remain exploratory. Overall, the available epidemiological evidence remains heterogeneous and influenced by methodological variability, underscoring the need for prospective investigations with standardized protocols in both domestic and wild feline populations to establish the true epidemiological and clinical significance of DCH.

SUGGESTION

The observed methodological heterogeneity highlights the need for further research employing standardized study designs and diagnostic approaches. Future studies should focus on harmonizing sampling strategies, specimen types and molecular diagnostic protocols to clarify temporal dynamics and true prevalence of DCH infection in cats. Additionally, enhanced molecular surveillance should be implemented in endemic regions to track DCH circulation patterns and inform targeted disease monitoring in both domestic and wild felid populations within the One Health framework.

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