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Bagaza Virus Emergence in Europe: Scoping Review of Transmission Dynamics, Phasianid Susceptibility, and Zoonotic Risks

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ABSTRACT

Bagaza virus (BAGV), a member of the Orthoflavivirus genus (Ntaya serocomplex), was first recorded in Europe, specifically in Spain, in 2010. Its natural transmission involves Culex mosquitoes as vectors and infected birds as reservoirs. Research has shown that BAGV can infect several game birds within the Phasianidae family. Antigenically, BAGV resembles other orthoflaviviruses within the Japanese encephalitis group, including West Nile virus (WNV) and Usutu virus (USUV), leading to possible cross-reactions when using less specific serological assays such as ELISA. Although significant animal health impacts have been described, aspects of transmission dynamics and zoonotic limits remain uncertain. Continued surveillance and research in high-risk regions are needed to enhance prevention and outbreak control. This paper presents a systematic review of BAGV findings across Europe.

Keywords: BAGV, Birds, Encephalitis, Orthoflavivirus, Red-legged partridge, Vector-borne infections

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Introduction

The Flaviviridae family consists of numerous unsegmented, positive-sense, single-stranded RNA viruses with genomes of roughly 10-11 kb, including major human pathogens like Dengue virus (DENV), Yellow Fever virus, and West Nile virus (WNV). A flavivirus genome comprises one open reading frame flanked by 5′ and 3′ untranslated regions, which encodes a polyprotein later processed into three structural proteins (C, prM, and E) and seven nonstructural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5) [1]. BAGV, classified under Orthoflavivirus (formerly Flavivirus, as renamed by the International Committee on Taxonomy of Viruses—ICTV) within the Ntaya serocomplex, follows an epidemiological cycle involving mosquitoes as vectors and birds as amplifying hosts [2]. Genomic analyses reveal close similarity between BAGV and the Israel turkey meningoencephalomyelitis virus (ITV) [3, 4], although the ICTV still treats them as separate entities [5].

BAGV was originally identified in 1966 in Bagaza, Central African Republic, from a pool of Culex mosquitoes [6]. Subsequently, it has been found in mosquito populations in Mauritania, Senegal [7], Namibia [8], and the United Arab Emirates [9]. Similar to other Orthoflavivirus members such as USUV [10], it later spread to Europe, where it was first detected in Spain in 2010—the first isolation from vertebrate hosts [11]. Since then, BAGV has been reported in several wild bird species [2, 11-14] and mosquito species [15].

Europe's ongoing climate shifts have contributed to unpredictability in vector-borne disease transmission. Rising temperatures and altered habitats influence mosquito populations, altering disease dynamics and triggering new outbreaks that may lead to millions of infections [16, 17]. In recent decades, flaviviruses transmitted by mosquitoes and maintained in avian hosts have expanded their range. DENV remains endemic in over 100 countries, particularly in Southeast Asia and the Western Pacific. USUV and WNV continue to appear in previously unaffected European regions [18, 19]. Mosquito breeding conditions enhance the likelihood of infection; mosquitoes acquire the virus from viremic hosts, and transmission can occasionally extend to incidental, dead-end hosts like humans and horses [18].

BAGV has been recognized as an emerging pathogen capable of infecting humans [20]. Serological evidence in humans has been reported [21], though its pathogenic potential in people remains unclear. Considering Europe already faces flavivirus-related illnesses such as tick-borne encephalitis and West Nile fever, both capable of inducing neurological disease [22], continuous monitoring is essential. BAGV's zoonotic potential remains poorly defined; thus, vector and virus surveillance can improve response efficiency and minimize health risks. This review compiles all available European BAGV records in a systematic manner.

Materials and Methods

This review includes all studies published before December 10, 2024, retrieved from PubMed, ScienceDirect, and Scopus. The analysis followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [23]. Only peer-reviewed, indexed papers written in English were considered. The search string applied was: (Bagaza OR BAGV) AND Europe. Articles were excluded if they did not involve BAGV detection in European countries. Two independent reviewers (FL and ACC) conducted screening and data extraction; disagreements were resolved through discussion.

The first step eliminated duplicate studies (n = 19). Only original research papers, letters, and short communications were retained, excluding 40 non-qualifying works. Additional filtering removed 43 irrelevant items. One French review was also found but excluded in the initial assessment; therefore, it was not included in the flowchart **(Figure 1)**. After applying inclusion and exclusion criteria, 12 publications were identified as suitable for detailed review **(Figure 1)**.

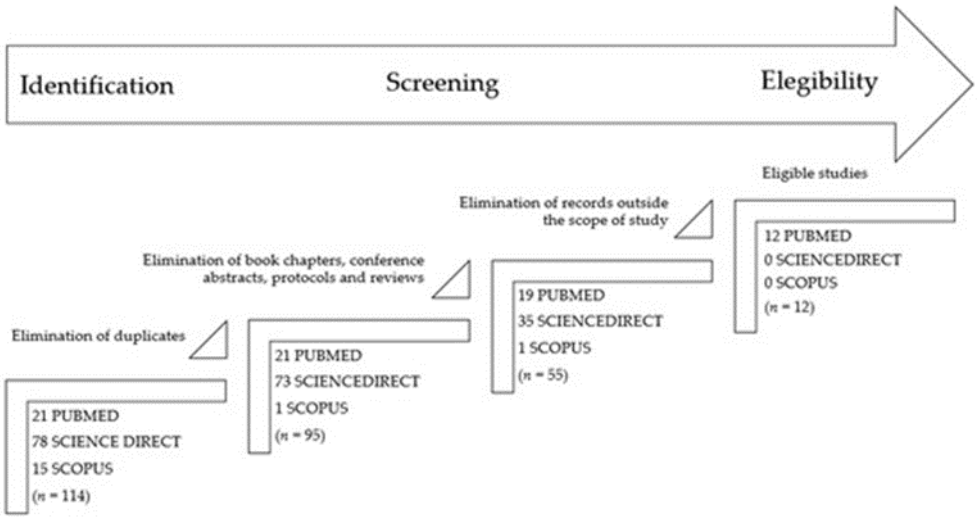

Figure 1. PRISMA diagram outlining the stages of record identification, screening, and the application of inclusion and exclusion criteria.

Results and Discussion

The initial database exploration retrieved 114 publications across the three selected sources. After excluding irrelevant works and fully reviewing the remaining papers, 12 studies met the eligibility requirements and were incorporated into this section. A synthesis of these publications is presented in **Table 1**.

Table 1. Overview of European studies documenting evidence of BAGV activity (organized by publication year).

Location	Sampling Date	Sample Type	Diagnostic Assay	Number of Positive/Total (%)	Sequencing (GenBank ID)	Species Identified with BAGV	Reference
Cadiz, Andalusia—Spain	September 2010	Tissues (heart, intestine, lung, liver, kidney, brain, and feathers)	RT-PCR (NS5 gene segment; segment 214 bp) Virus isolation (AF, CM, ECE, VS)	13/13 (100)	HQ644143 HQ644144	Alectoris rufa; Phasianus colchicus	[11]
Cadiz, Andalusia—Spain	September 2010 2010-2011	Tissues (heart, intestine, lung, liver, kidney, brain, and feathers)	qRT-PCR (NS5 gene)	11/11 (100) 0/81 (0)		Alectoris rufa	[24] 1
Southwestern Spain	August 2010	Oropharyngeal and cloacal swabs Tissues (brain, oral mucosa, pectoral muscle, trachea, lung, heart, liver, spleen, pancreas, duodenum, caecal tonsils, kidney, bursa of Fabricius, thymus and skin with feather follicles)	qRT-PCR Immunohistochemistry	13/13 (100)	AY632545.2	Alectoris rufa; Columba palumbus; Phasianus colchicus	[12]
Cadiz, Andalusia—Spain	August-October 2010	Blood Tissue samples Oropharyngeal and cloacal swabs	RT-PCR	11/14 (78.6)		Alectoris rufa; Phasianus colchicus	[25]
Cadiz, Andalusia—Spain	October 2011-February 2012	Serum Brain	VNT RT-PCR	25/172 (14.5) 0/172 (0)		Alectoris rufa; Phasianus colchicus	[26]
France	September 2009-	Blood	VNT	0/73 (0)		Capreolus capreolus	[27]

	February 2010					; Sus scrofa	
Extremadura—Spain	October 2017-December 2019	Tissues (blood, brain, heart, intestine, liver, lung, muscle, kidney, spleen, stomach, pancreas and the pulp of immature feathers)	VNT	0/157 (0)	---		[28]
Serpa, Alentejo—Portugal	September 2021	Tissues (feather pulp, brain, heart, kidney, spleen, and intestine) Growing feathers (live birds)	qRT-PCR (NS2b, NS5, and 3′ NT region)	9/12 (75) 4/30 (13.3)		Alectoris rufa; Emberiza calandra	[14]
Cadiz, Andalusia—Spain	October 2019	Growing feathers, heart, brain, liver, spleen and kidney; Tissues (heart, brain, spleen, liver, kidney, lung, skeletal muscle, skin, cecal tonsils, adrenal glands, gonads and pancreas	qRT-PCR (NS5 gene segment; partial segment 222 bp) Immunohistochemistry	4/4 (100)	OK424741 OK424742	Alectoris rufa	[29]
Cadiz, Andalusia—Spain	October 2019-August 2021	Brain	qRT-PCR (NS5 gene segment) Virus isolation (Vero and BSR cells)	4/4 (100)	PP236854 PP236853 PP236852 PP236851	Alectoris rufa	[30]
Mértola, Alentejo—Portugal	September 2023	Tissues (kidney, spleen, heart and feather follicles)	qRT-PCR (NS5 gene; 342 bp region within the NS1 gene)	4/7 (57.1)	PP130723	Pica pica	[2]
Cadiz and Seville, Andalusia—Spain	July 2021-February 2022 January-December 2021	Tissues (brain, growing feathers) Oropharyngeal and	RT-PCR (NS5 gene)	32/89 (35.9) 4/215 (1.9)	PP887449 PP887448 PP887447 PP887446 PP887445 LC730845	Alectoris rufa; Phasianus colchicus Picus viridis;	[31]

	cloacal swabs		Platalea leucorodia; Ciconia ciconia; Aegypius monachus

Abbreviations: AF—Allantoic fluid; CM—Chorioallantoic membrane; ECE—Embryonated chicken egg; NS—Nonstructural; NT—Nontranslated; qRT-PCR—Quantitative reverse transcription PCR; VNT—Viral neutralization test; vs.—Viscera. [1] Methodology-based study; does not confirm virus occurrence but describes assay development.

Conclusion

Most of the research originated from Spain (n = 9), followed by Portugal (n = 2) and France (n = 1). Of these, 11 papers involved detections in birds, while one study referred to infections in ungulate mammals [27]. Within the avian group, the order Galliformes was predominant, particularly the family Phasianidae. The Red-legged Partridge (Alectoris rufa) appeared in nine investigations, and the Common Pheasant (Phasianus colchicus) in five. Data suggest that BAGV primarily affects phasianids, several of which are globally recognized game species [32]. The virus has also been noted in the Himalayan Monal (Lophophorus impejanus) [13], and experiments demonstrated that Grey Partridges (Perdix perdix) are vulnerable to BAGV-induced neurological syndromes [33]. Single studies reported infection in other avian taxa, including the Corn Bunting (Emberiza calandra) [14], Cinereous Vulture (Aegypius monachus) [31], Common Woodpigeon (Columba palumbus) [12], Eurasian Magpie (Pica pica) [2], Eurasian Spoonbill (Platalea leucorodia), Green Woodpecker (Picus viridis), and White Stork (Ciconia ciconia) [31]. Experimental infection of House Sparrows (Passer domesticus) failed to produce clinical signs, viremia, or mortality [34]. Presently, evidence indicates no particular susceptibility pattern outside game birds [34], though sample numbers are too limited for firm conclusions. However, species behavior—such as frequenting mosquito-rich habitats—could increase exposure risk.

Typical clinical manifestations of BAGV infection include marked weight loss, lethargy, weakness, limited mobility, and neurological abnormalities such as paralysis, disorientation, ataxia, lack of responsiveness, and occasionally circling movements or neck twisting [25, 33, 34]. Beyond its neurotropic nature, BAGV shows affinity for endothelial cells, triggering severe hemolytic events [35]. In Spain and Portugal, where cases are most frequent, veterinarians should consider BAGV in the differential diagnosis of birds showing hemolytic anemia of uncertain cause.

Reported mortality rates range between 30-40%, occurring approximately 6-10 days post-infection (dpi). Viremia typically appears between 3-5 dpi, peaking at 3 dpi during experimental observation. Neutralizing antibodies were measurable in all partridges by 7 dpi [33, 34]. Viral shedding began at 3 dpi and persisted until 11 dpi, detected via cloacal and oral routes. Among diagnostic samples, oropharyngeal swabs yielded the most consistent detection, whereas feathers allowed RNA identification at later stages, even after the virus was no longer detectable in blood or swabs [34]. For postmortem diagnosis, brain tissue is recommended, as it frequently tests positive in confirmed cases [13]; in multiple reports, nearly all tested organs were positive in brain samples [11, 12, 24].

Both the Japanese encephalitis (JE) and Ntaya groups within Orthoflavivirus encompass neurotropic viruses infecting a range of vertebrates. Because these agents share an ecological cycle involving Culex mosquitoes and avian hosts, co-circulation in nature is plausible [36, 37]. Within the JE complex, WNV and USUV are notable in Southwestern Europe. Antibodies elicited by these viruses and BAGV can cross-react in serological assays, leading to false positives [38]. While ELISA serves as an initial screening test, VNT remains the confirmatory method of choice for higher specificity—though some cross-reactivity persists, particularly between WNV and USUV [38, 39].

For molecular detection, RT-PCR-based assays are standard. Broader assays capable of detecting viral species from both serocomplexes within a single reaction enhance diagnostic precision. A quantitative duplex qRT-PCR system has been proposed as a sensitive and specific diagnostic approach for simultaneous monitoring of JE and Ntaya orthoflaviviruses in avian surveillance [37]. Another effective method is qRT-PCR targeting the BAGV

NS5 gene [24]. Establishing surveillance frameworks under national authority oversight would help assess the periodic prevalence of each Orthoflavivirus and strengthen public and veterinary health preparedness.

The complete genome sequence of Bagaza virus (BAGV) was obtained many years ago [40]. Genetic comparison of the first Spanish isolate demonstrated a closer relationship to the African strain than to the one identified in India [11]. It has been suggested that migratory birds could facilitate intercontinental transmission of BAGV, as observed for other flaviviruses, although this hypothesis remains unverified [41, 42]. A recent genomic study of the Portuguese isolate revealed a phylogenetic connection to the Spanish lineage, implying that cross-border dissemination was the most likely introduction pathway [4]. This finding holds ecological importance, particularly because the Iberian Peninsula is home to several endangered and endemic species. Therefore, any shared biological threat affecting Spain and Portugal should be managed collaboratively, considering the genetic and conservation value of their vulnerable wildlife populations.

In summary, the Red-legged Partridge has proven to be an appropriate indicator species for BAGV monitoring. Expanded epidemiological investigations on susceptible bird populations are essential to better understand and control the emergence, persistence, and transmission of this pathogen. Implementing active surveillance programs with broad-scale sampling of free-ranging birds would improve early detection. Given its presence in the Iberian Peninsula, an area classified as high risk, BAGV poses a potentially escalating threat to wild avifauna—making preventive action the most effective strategy for mitigation.

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