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Short communication

Genomic Characterization of Lumpy Skin Disease Virus in Sardinia, Italy 2025

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Abstract

Lumpy Skin Disease virus (LSDV) is a *Capripoxvirus* that causes Lumpy Skin Disease (LSD), a highly contagious disease of cattle transmitted primarily by blood-feeding arthropods, but also through direct contact and fomites. On 20 June 2025, an outbreak was reported in a beef cattle farm in Orani (Nuoro, Sardinia, Italy), where 21 of 131 animals showed typical clinical signs. Fourteen samples tested positive for LSDV by real-time PCR, and selected specimens underwent whole genome sequencing, generating three high-quality consensus sequences. Phylogenetic analysis placed the Sardinian strains within clade 1.2, closely related to a Nigerian isolate from 2018 and clearly distinct from vaccine-derived strains and those responsible for the Balkan outbreaks between 2012 and 2016. LSD outbreaks also occurred in North Africa during 2023–2024, but genomic data from those episodes are not yet available for comparison. The exact route of introduction into Italy therefore remains uncertain, with possible pathways including windborne dispersal of infected vectors or other anthropogenic activities. This first genomic characterization of LSDV in Italy highlights the need for strengthened genomic and entomological surveillance, data sharing, and integrated approaches to trace virus incursions and assess transboundary risks.

Keywords

Lumpy skin disease, Genomic characterization, Disease Surveillance, Phylogenetic analysis

Short communication

Lumpy Skin Disease virus (LSDV) is a double–stranded DNA virus of the species *Capripoxvirus lumpyskinpox*, genus *Capripoxvirus* within the subfamily *Chordopoxvirinae*, family *Poxviridae* (https://ictv.global/report/chapter/poxviridae/poxviridae/capripoxvirus, last accessed on August 28, 2025).

LSDV primarily infects cattle, water buffaloes, and certain wild ruminants, causing Lumpy Skin Disease (LSD), a highly contagious viral disease characterized by extensive cutaneous nodules, fever, regional lymphadenopathy, nasal, ocular discharge. Transmission occurs mainly via blood-feeding arthropods, including biting flies, mosquitoes, and ticks; however, direct contact with infected animals, exposure to infectious secretions, and contaminated fomites also contribute to viral spread (Tuppurainer et al., 2012). The primary risk factors for LSD dissemination are linked to the introduction of the virus via blood-feeding insects over short distances and through both legal and illegal animal movements over longer distances (Bianchini et al., 2023). Windborne dissemination of infected vectors has also been proposed as a possible pathway in certain epidemiological contexts (Klausner et al., 2017; Hall et al., 2023).

LSD results in substantial economic losses due to reduced productivity (milk yield and weight gain), trade restrictions, and the costs associated with control measures. Early detection and rapid response are critical for outbreak containment, while vaccination remains a cornerstone of preventive strategies to limit viral transmission, it also plays a

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crucial role in markedly reducing the occurrence and severity of clinical disease in the field (Tuppurainer et al., 2012).

On 20 June 2025, clinical suspicion of LSD was reported on a large beef cattle farm in the municipality of Orani, province of Nuoro, Sardinia. The farm housed 131 Sardo Bruna cattle, of which 21 animals (16%) exhibited fever, ocular and nasal discharge, lymphadenopathy, hypersalivation, and characteristic cutaneous nodules. Fourteen biological samples including EDTA-blood, serum, saliva, and conjunctival and oral swabs were collected from three symptomatic animals by the official veterinary services of the Azienda Sanitaria Locale-3 (ASL-3, Nuoro). Initial screening at the Istituto Zooprofilattico Sperimentale della Sardegna (Sassari, Italy) was performed using a real-time PCR assay targeting *Capripoxvirus* DNA (Bowden et al., 2008), and all 14 samples turned out positive. These samples were then sent to the National Reference Centre for Exotic Diseases (CESME) at the Istituto Zooprofilattico Sperimentale dell'Abruzzo e del Molise (IZSAM, Teramo, Italy) for confirmatory testing. A real-time PCR assay specific for LSDV (Bio-T kit®, Biosellal, France) confirmed the 14 samples as positive, with cycle threshold (Ct) values ranging from 23 to 35.

Following confirmation, the outbreak was promptly notified to the Italian Ministry of Health by the Official Veterinary Service of ASL-3 of Nuoro, by means of the Sistema Informativo Malattie Animali-SIMAN information system, which subsequently notified the European Commission and World Organization for Animal Health in accordance with current regulations. A vaccination program targeting all cattle in the island started one month after the confirmation of the first case, using the live attenuated vaccine for cattle (LSD Neethling strain) produced by Onderstepoort Biological Products, the only commercial vaccine authorized under derogation by the European Commission according to Regulation (EU) 2019/6.

Five samples including saliva, EDTA-blood and serum with the lowest Ct values were selected for whole genome sequencing. DNA was extracted by MagMAX™ CORE Nucleic Acid Purification Kit (Applied Biosystems™, Waltham MA, USA) following manufacturer's instructions and libraries were prepared using the Illumina DNA Prep Kit (Illumina Inc., CA, USA). Sequencing was performed on the NextSeq 1000 platform with the NextSeq™ 1000/2000 P2 XLEAP-SBS™ Reagent Kit (300 cycles) generating paired-end reads of 150 bp in length (Illumina Inc., CA, USA). Each sample produced between 18 and 37 million raw reads, with an average Phred quality score of 38.

Bioinformatic analysis was conducted using the GENPAT platform (https://genpat.izs.it/). Reads were mapped to the LSDV NI-2490 reference genome (Neethling 2490 isolate, National Center for Biotechnology Information database under accession number (NCBI acc. no) AF325528.1) using iVar tool (v1.4.4, Grubaugh et al., 2019). Among the five selected samples, we chose for downstream analysis the sequence obtained from the saliva sample (ID: 2025.TE.13092.1.1), which yielded a consensus genome with 98.41% horizontal coverage and an average vertical coverage of 5.9×. This sequence was subsequently released on NCBI with acc. no. PX222718.

On 27 June 2025, a head of cattle that had recently been moved from the affected farm in Nuoro to a facility in Bottida, province of Sassari, also showed clinical signs consistent with LSD. PCR testing confirmed infection, and the animal was culled on 30 June 2025. Tissue samples from lymph nodes, lung, spleen, and skin nodules were collected and submitted to IZSAM for genomic analysis as previously described. The skin nodule sample (ID: 2025.TE.14371.1.1) produced the highest-quality genome, with 99.66% horizontal coverage and 6.78× vertical coverage (NCBI acc. no. PX222719). Virus isolation from this sample was also performed on continuous foetal lamb testis cells (OA3.Ts, Di Felice et al., 2024). The viral isolate LSDV ITA2025 (ID: 2025.TE.18152.1.1) was obtained after two cell passages and then sequenced and analyzed as previously described. A complete consensus genome sequence of 150,879 bp in length with Vcov of 49.9x was produced (NCBI acc. no. PX222720).

Phylogenetic reconstruction was performed using the Auspice toolkit (v2.53.0, Hadfield et al., 2018) integrated within the GENPAT platform. Maximum likelihood trees generated with IQ-TREE, based on a curated set of representative LSDV genomes (Van Borm et al., 2023), placed all three Sardinian LSDV sequences within clade 1.2, which includes field isolates (Figure 1). A further analysis, based on the complete sequence of the LSDV ITA2025 isolate (ID: 2025.TE.18152.1.1) and related clade 1.2 sequences available in the NCBI database, revealed a close relationship between the Sardinian strain and the LSDV isolate V281 (Nigeria 2018, NCBI acc. no. OK318001.1). In contrast, the sequences of strains responsible for LSD outbreaks in the Balkans (Albania, Greece, Serbia, Bulgaria, and North Macedonia), as well as in Russia, Turkey, and Israel during 2012–2016 (Menasherow et al., 2014; Mercier et al., 2018; Sprygin et al., 2018), clustered separately (Figure 2, top clade and its sister clade composed of Russian sequences).

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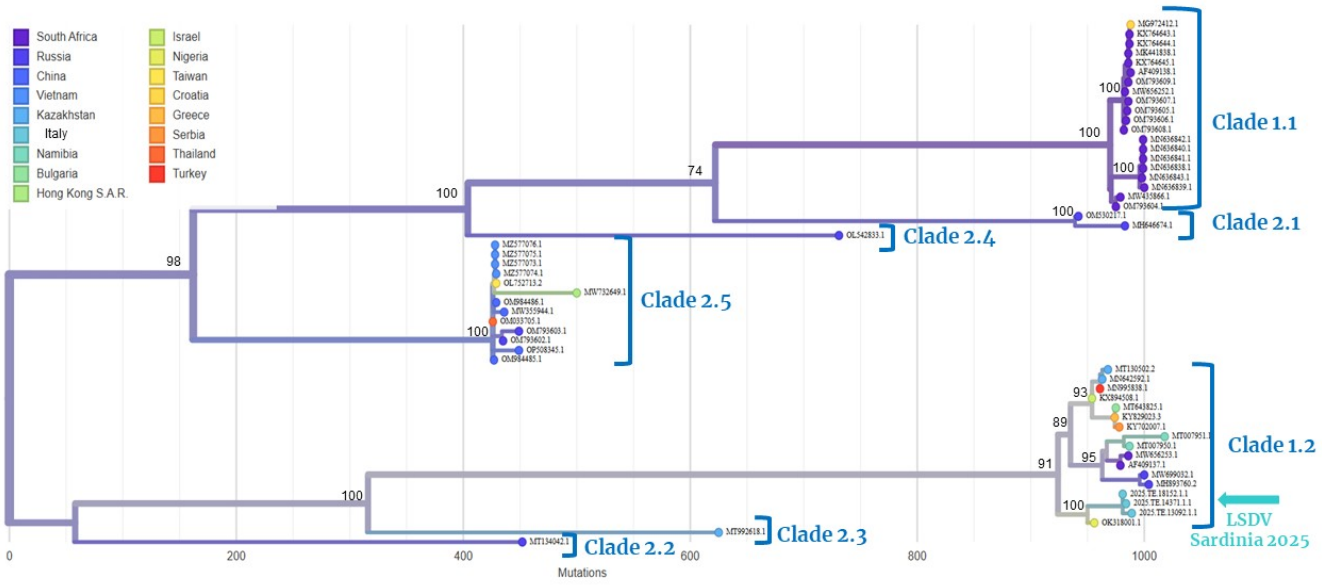

Figure 1. Maximum Likelihood tree obtained by IQ-TREE for LSDV Clade assignment. Clade 1.1: LSDV Neethling-like/vaccines strains group, Clade 1.2: LSDV wild-type strains group, Clade 2.1-2.5: LSDV recombinant strains group originated from a Neethling-like virus. Confidence values higher than 70% were showed. LSDV Sardinian 2025 sequences 2025.TE.13092.1.1, 2025.TE.14371.1.1 and 2025.TE.18152.1.1 were released on NCBI with accession numbers PX222718, PX222719, and PX222720, respectively.

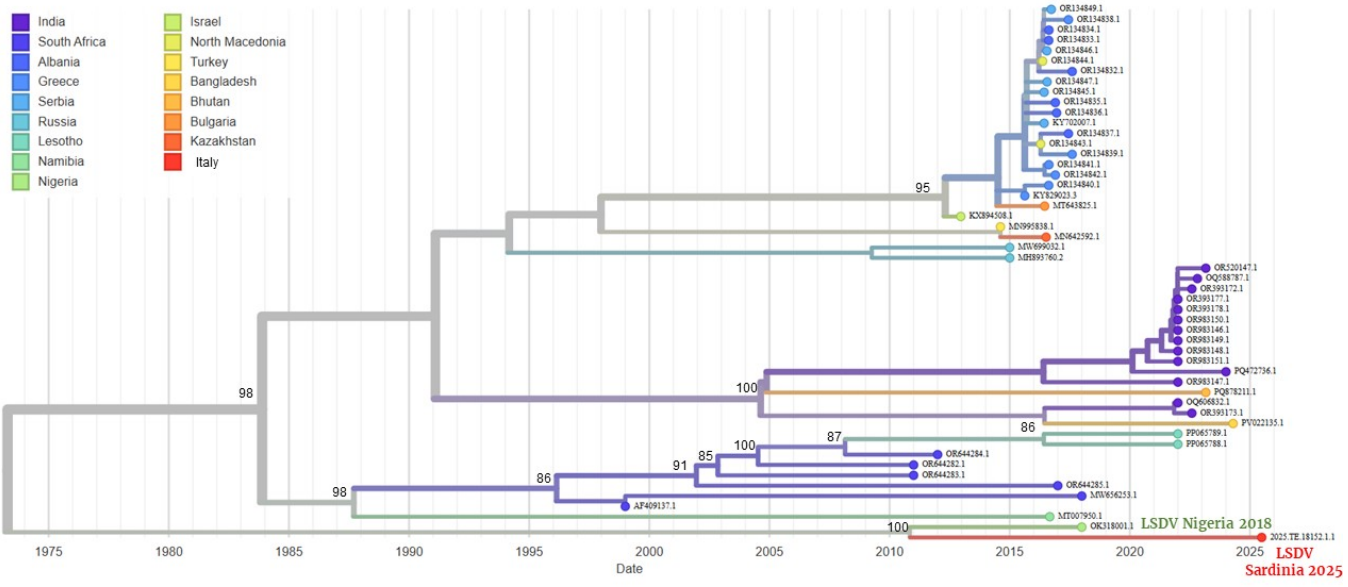

Figure 2. Maximum Likelihood tree obtained by IQ-TREE with the LSDV ITA2025 isolate (LSDV Sardinia 2025- ID: 2025.TE.18152.1.1, NCBI accession number PX222720) and field strains belonging to clade 1.2 from Turkey, Israel, Russia, and Balkans - Greece, Albania, Serbia, Bulgaria and North Macedonia - (top clades), Indian subcontinent (central clade) and Africa (bottom clade). Confidence values higher than 70% were showed.

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Conclusion

This report presents the molecular characterization of the LSDV strain responsible for the Sardinian outbreak which started in June 2025. Genomic analyses identified the virus as a field strain belonging to clade 1.2, closely related to a Nigerian isolate from 2018, and clearly distinct from vaccine-derived strains as well as from those that caused outbreaks in the Balkans a decade ago. These findings support an African origin for the strain detected in Italy. However, the precise origin and mode of introduction of LSDV into Sardinia in 2025 remain still unclear. In 2023–2024, LSD cases were reported in Libya, Algeria, and Tunisia (Mejri and references therein), although genomic data from these outbreaks are not yet available for comparison. Several introduction routes are currently under consideration. As previously documented for other vector-borne viruses such as Bluetongue virus (Lorusso et al., 2017; Cappai et al., 2019) and Epizootic Hemorrhagic Disease virus (Sghaier et al., 2022; Lorusso et al., 2023), windborne dispersal of infected vectors from North Africa could represent one plausible pathway. Other pathways of virus introduction related to anthropogenic activities cannot be excluded at this stage. This uncertainty highlights the need to integrate entomological, epidemiological, and genomic data to better understand the pathways of LSDV spread. To date, confirmed cases of LSDV have also been reported in France, involving 77 outbreaks across 42 livestock farms and 13 municipalities. The source of infection remains undetermined, and epidemiological investigations are ongoing (https://wahis.woah.org/#/in-review/6584).

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Ethical approval

No ethical approval was required for this study

Conflict of interest

The authors declare no conflict of interest

Author Contributions

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All authors have read and agreed to the published version of the manuscript.

Data availability

The sequences were submitted to the NCBI database with the following accession numbers PX222718, PX222719 and PX222720.

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