

## Diagnostic and pathological characterization of senecavirus A-associated epidemic transient neonatal losses in swine

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### Key Points:

- SVA detection was associated with diarrhea and increased mortality in neonatal pigs.
- SVA localizes preferentially in lymphoid tissues, suggesting possible lymphoid replication and immune involvement.

### Introduction

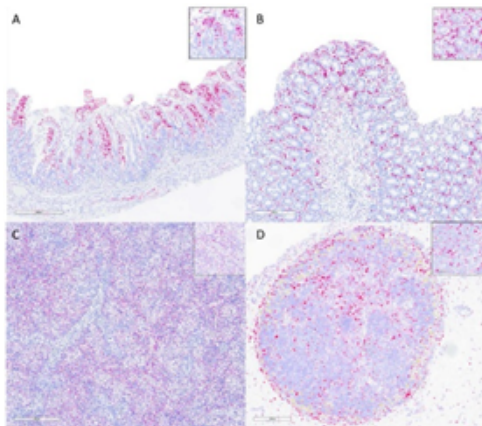
Senecavirus A (SVA) is an emerging swine picornavirus historically associated with idiopathic vesicular disease but more recently linked to epidemic transient neonatal losses (ETNL) in piglets. ETNL is characterized by a sudden increase in neonatal mortality with nonspecific clinical signs. Despite increasing recognition of SVA as an emerging pathogen, the pathological mechanisms and tissue tropism in affected neonatal pigs remain poorly defined. This study aimed to retrospectively characterize the clinical, molecular, and pathological features associated with SVA infection in cases of neonatal swine mortality, using RT-qPCR, histopathology, *in situ* hybridization (ISH), and immunohistochemistry (IHC).

### Methods

A retrospective analysis was conducted on 186 diagnostic submissions comprising 324 individual piglets (<24 days of age) tested for SVA by RT-qPCR at the Iowa State University Veterinary Diagnostic Laboratory. Clinical history, gross pathological findings, and microbiological results were collected. Selected tissues were evaluated by RNAscope® ISH and IHC to localize viral RNA and assess co-infection status, especially with Rotavirus A and C. Clinical and diagnostic data were compared between SVA-positive (n = 71) and SVA-negative (n = 253) cases.

### Results

In this retrospective study of 186 neonatal swine submissions tested for Senecavirus A (SVA), the virus was detected by RT-qPCR in 21.9 % of cases, with the highest viral loads found in feces, serum, and especially spleen tissue, suggesting a preference for replication in lymphoid tissues ( $p < 0.05$ ). *In situ* hybridization (Fig. 1) confirmed the presence of viral RNA in spleen, lymph nodes, and lymphoid aggregates in the intestine, supporting this lymphoid tropism. Clinically, increased mortality was strongly associated with SVA detection ( $p < 0.001$ ). Co-infections were common, with 28.2 % of SVA-positive animals being positive for Rotavirus A, while other pathogens such as Rotavirus C and bacterial agents were detected across both SVA-positive and negative groups. Notably, respiratory pathogens, including *Streptococcus suis*, *Actinobacillus suis*, and *Streptococcus equisimilis* were significantly more frequent in SVA-positive piglets ( $p < 0.01$ ), indicating possible immune compromise or multifactorial disease processes. Despite a short systemic viremia, the persistence of SVA in lymphoid tissues and its association with neonatal losses highlight its role in epidemic transient neonatal mortality in swine.



**Fig. 1.** Tissue distribution of SVA nucleic acid detection by *in situ* hybridization: (A) Small intestine, showing strong and diffuse SVA nucleic acid labeling within the lamina propria; the inset shows higher magnification highlighting distinct labeling of lymphoid aggregate. (B) Colon with scattered SVA-positive cells localized within the lymphocytes of the lamina propria and submucosa; inset highlights positive lymphocytes at higher magnification. (C) Spleen demonstrating widespread positive SVA labeling within the white pulp; inset shows detailed labeling within periarteriolar lymphoid sheaths and adjacent follicles. (D) Lymph node with SVA hybridization signal predominantly in the medullary region and along the follicular periphery; inset: highlights SVA-positive cells within germinal centers.

### Discussion

The study provides new insights into the role of SVA, demonstrating its frequent detection in cases of neonatal mortality. Although diarrhea appears to be one of the most common clinical signs reported in ETNL cases, SVA was most frequently detected in intestinal lymphoid tissues rather than causing atrophic enteritis, suggesting that enteric signs are likely the result of concurrent co-infections. The localization of viral RNA to lymphoid tissues underscores a likely role of immune-associated replication and potential immunosuppression. Frequent co-infections complicate lesion interpretation and suggest that while SVA contributes to neonatal disease, multifactorial processes are likely involved. Overall, these findings highlight the importance of integrated clinical, molecular, and histopathological diagnostics to confirm ETNL clinical cases and understand SVA pathogenesis and its role in ETNL. Future studies should further explore host immune responses and interactions with co-pathogens to fully elucidate mechanisms of neonatal mortality.

**Reference:** Eduarda Ribeiro Braga, Emanoelly Machado Sousa da Silva, Anderson Hentz Gris, Jennifer Groeltz-Thrush, Pablo E. Piñeyro, Diagnostic and pathological characterization of senecavirus A-associated epidemic transient neonatal losses in swine, *Microbial Pathogenesis*, Volume 212, 2026, 108303, ISSN 0882-4010, <https://doi.org/10.1016/j.micpath.2026.108303>.