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FATAL MPOX CASES IN UGANDA: GENOMIC DEEP SEQUENCING TO EXPLORE CO-MORBIDITIES AND RISK FACTORS

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BACKGROUND

- In November 2025, 50 deaths were recorded among confirmed mpox cases in Uganda
- HIV co-infection was present in 46% of the cases
- Mortality occurred equally among males and females
- Age distribution differed by sex:
  - 72% of male deaths occurred in persons <30 years
  - 68% of female deaths occurred in persons >30 years

(1) HIV is a major co-morbidity in fatal mpox cases and viral co-infections such as Varicella Zoster Virus (VZV) may further increase disease severity and mortality

(2) Bacterial co-infections were common and strongly associated with secondary infections and sepsis-related complications

(3) Fatal mpox in Uganda is strongly associated with HIV infection, VZV co-infection, bacterial superinfection and AMR-related sepsis

METHODS

Cross sectional study

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Referral hospitals (Entebbe, Mbarara, Kawolo, Hoima)

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Laboratory confirmed (PCR) mpox cases

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22 Fatal Mpox cases genotyped

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Target enrichment next-generation sequencing (NGS) – Illumina MiSeq

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Metagenomic in-house and DRAGEN bioinformatics analysis pipelines

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Antimicrobial Resistance (AMR) profiling

RESULTS

VZV & HIV CO-INFECTIONS

22 — Total MPXV Samples — Successfully sequenced

17/22 — VZV Co-infections — 77.3% overall

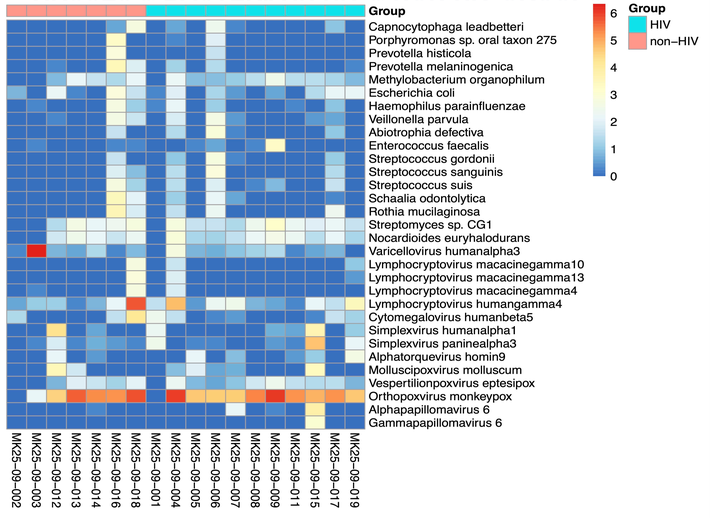
9/11 — VZV in HIV+ — 81.8% co-infection

4/7 — VZV in HIV- — 57.1% co-infection

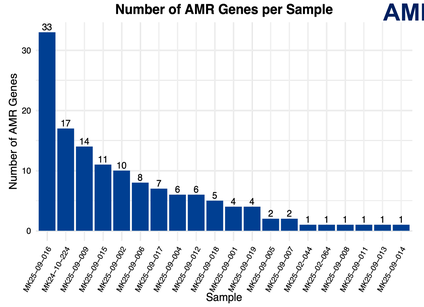
4/4 — VZV in Unknown HIV Status — 100% co-infection

Fisher's exact test
- Odds ratio = 2.14
- 95% CI = 0.12 - 40.24
- P Value = 0.584

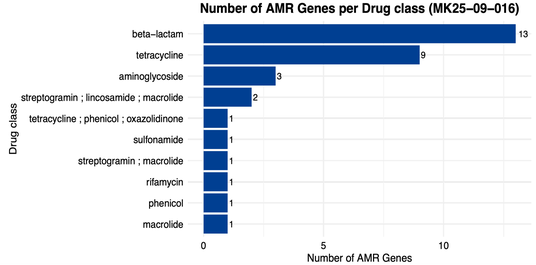
VIRUSES & BACTERIA IN HIV & NON-HIV GROUPS



Number of AMR Genes per Sample



AMR GENES IN HIV POSITIVE CASES



CONCLUSIONS

- A diverse microbial profile characterizes fatal mpox cases
- Key co-morbidities such as HIV and VZV infections were frequent and likely contribute to disease severity and mortality
- Bacterial co-infections included *Staphylococcus aureus, Staphylococcus haemolyticus, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Streptococcus pyogenes* and *Acinetobacter baumannii*
- HIV-positive individuals exhibited a markedly higher AMR gene load
- AMR genes mostly conferred resistance to *β-lactams, tetracyclines, aminoglycosides and macrolides were identified*
- Secondary bacterial infections and sepsis are major contributors to adverse clinical and mortality outcomes

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