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Poster Session I

Basic science: pathogenesis of staphylococci

COMMUNITY-ASSOCIATED MRSA STRAINS ARE NO MORE VIRULENT THAN HEALTHCARE-ASSOCIATED MRSA STRAINS IN A RANGE OF LABORATORY ASSAYS

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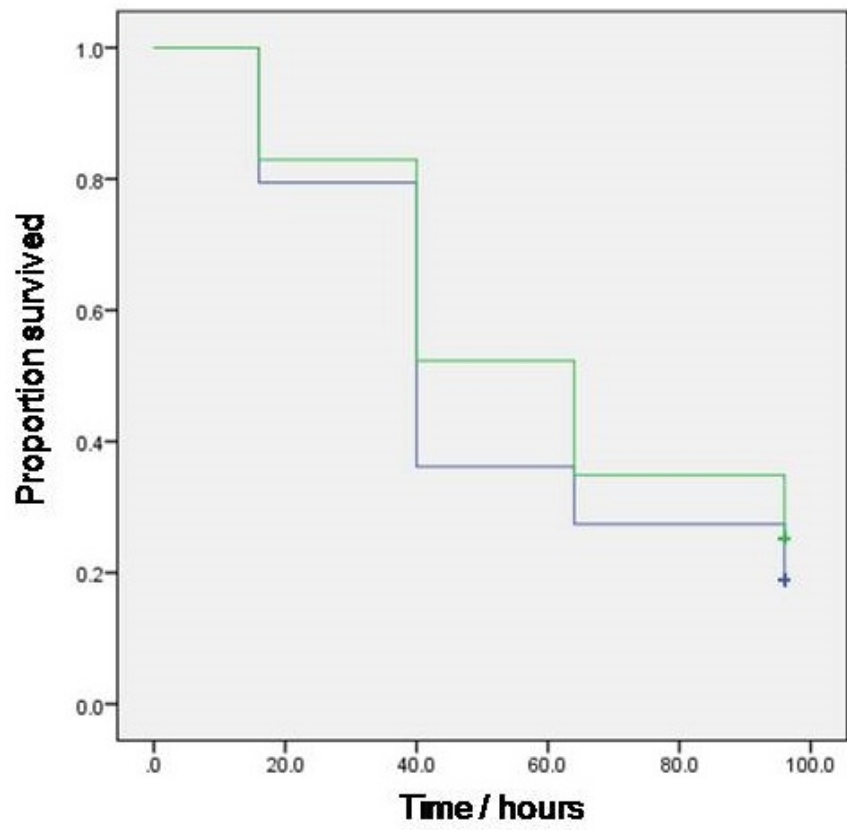
Objectives: Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) have emerged globally in the past decade and are associated with more severe disease than healthcare-associated MRSA (HA-MRSA). This study compares the virulence of CA- and HA-MRSA strains in a range of laboratory assays.

Methods: Eighteen HA-MRSA strains (ST22-IV (EMRSA-15) and ST36-II (EMRSA-16)) and 26 CA-MRSA strains (ST1-IV (PVL+ USA400), ST1-IV (PVL-), ST8-IV (USA300), ST22-IV (PVL+), ST30-IV, ST59-IV and ST80-IV) were selected from our local collection. Fibrinogen and fibronectin binding by CA and HA strains in exponential and stationary phases was compared using t-tests. A *Galleria melonella* (caterpillar) pathogenicity model was performed and differences compared using survival analysis and the log-rank test. Phenol Soluble Modulin (PSM) production was measured using mass spectrometry and compared using ANOVA. *agr* (accessory gene regulator) expression was measured in 5 and 10 hour cultures using realtime PCR and compared using ΔC_T methodology with *gyr* as a reference. *agr* expression was tested for at least one representative strain from each clone; the other assays were performed on all strains.

Results: Overall binding to fibrinogen and fibronectin was significantly lower for CA vs HA strains in exponential and stationary phases ($p < 0.05$), but there was no difference in binding to fibrinogen and fibronectin moving from exponential to stationary phase ($p > 0.05$). There was no significant difference in overall PSM production between HA and CA strains ($p = 0.231$) but there was significant variation between clones ($p = 0.003$). Surprisingly, *G. melonella* caterpillar mortality was significantly higher in HA vs CA strains ($p = 0.007$) (Figure), and there was a significant difference between clones ($p < 0.001$). There was a significant negative correlation between mean PSM production and mean caterpillar survival time ($r^2 = 0.70$, Pearson's Correlation $p = 0.01$). There was a significant reduction in *agr* expression in 10 vs 5 hour cultures from CA ($p = 0.002$) but not for HA strain ($p = 0.304$).

Conclusion: There are significant differences in activity of MRSA strains in laboratory assays that model distinct steps in the pathogenesis of *S. aureus* disease; however we did not identify a consistent and distinct virulence phenotype for the CA vs HA group. The mechanism of increased disease severity attributed to CA-MRSA remains unclear and may not be applicable to all epidemiologically defined clones.

Figure. Kaplan-Meier plot of *Galleria melonella* caterpillar survival following infection with healthcare-associated vs community-associated MRSA. A log-rank test indicates significantly increased virulence in healthcare-associated vs. community-associated strains ($p = 0.007$).



Green = CA strains.
Blue = HA strains.