Genomic insights into national surveillance of MRSA bacteraemia in England

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INTRODUCTION

The MRSA bacteraemia prevalence in England has been stable at <9% since 2012

Cases are mandatorily reported, but information on the molecular epidemiology is lacking

We sought to merge the strengths of molecular and clinical epidemiology by:

- Expanding existing data collection systems to include whole-genome sequencing (WGS) of isolates from all cases of MRSA bacteraemia in England
- Combining patient-level and genomic data to better understand the epidemiology and help support the development of interventions to further reduce MRSA rates

METHODS

Between April 2017 and March 2018, laboratories throughout England were invited to refer MRSA from bacteraemia cases to the National Infection Service (Public Health England, London) for analysis

Samples were matched with mandatory surveillance data using patient identifiers

Cases occurring ≥3 days after admission were defined as hospital-onset (HO-MRSA); the remainder as community-onset (CO-MRSA)

MLST, SCC*mec* type, toxome and resistome data were derived from WGS as described previously[1,2]; genetic relatedness was assessed by hierarchical clustering

MRSA were considered multi-drug resistant (MDR) when genotypically resistant to β-lactams and ≥2 other classes of antibiotic

RESULTS

- 846 MRSA bacteraemia cases were reported nationally between April 2017 and March 2018
- Of these, 644 (76%) were deterministically linked with WGS data and studied further
- The median age was 64 years (range 0-102); cases among males were more common (66%) [Fig 1]
- >70% cases in each region were studied indicating broad geographic coverage [Fig 2]
- Most (430; 67%) were defined as CO-MRSA
- MRSA were genotypically diverse: at least 19 different MLST-clonal complexes and 12 SCC*mec* (sub)types were identified [Fig 3]
- CC22 and CC5 were the most frequent clonal groups (48% and 17% respectively), but multiple SCC*mec* types indicate additional underlying heterogeneity [Fig 3]
- CC22-IVh (EMRSA-15 *sensu stricto*)[3] predominated (212; 33%) and occurred in all 9 regions
- Despite being a classical HA-MRSA clone, 123 (58%) E-15 cases were CO-MRSA
- CC5-IVg was the second most common lineage (45; 7%) and was frequently defined as CO-MRSA (36; 80%)
- Phylogenetic analyses and risk factor data provided evidence of clonal expansion of CC5-IVg in the South West of England, frequently associated with PWID [Fig 4]
- 68 (10.6%) were PVL-positive , belonging to 12 distinct lineages
- 18 USA300 cases (2.8% all cases) were identified
- Genotypically, 65.7% (423) were MDR; decreased susceptibility to decolonisation agents was less common (*mupA* 4%; *qacA/C* 15.5%)

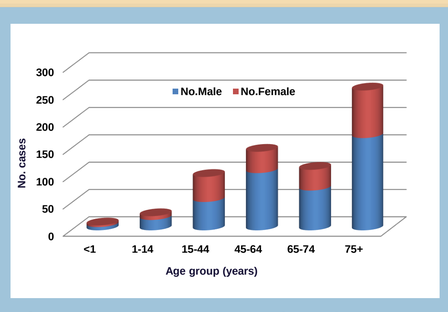

Figure 1. Age and gender of cases

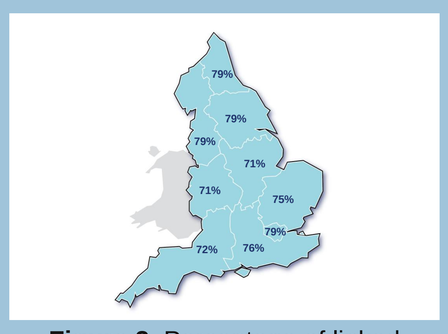

Figure 2. Percentage of linked cases by region

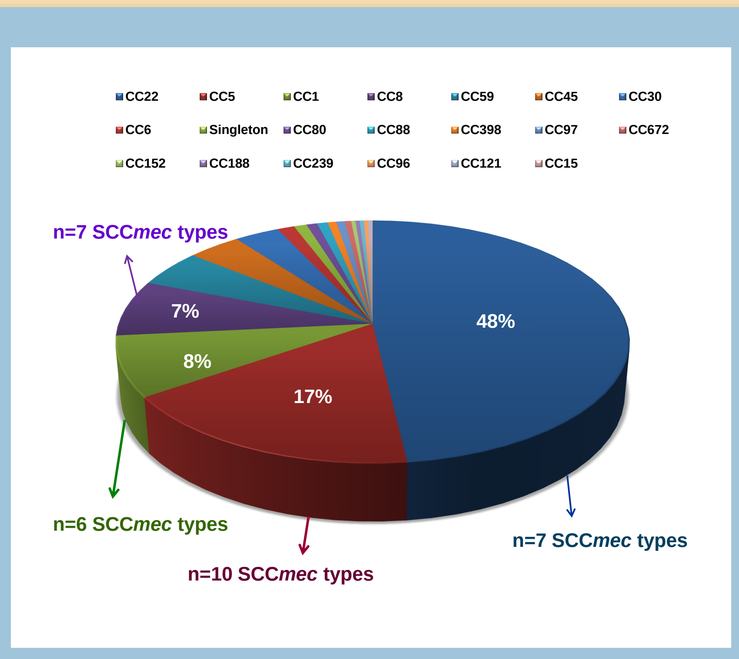

Figure 3. Genetic diversity among MRSA bacteraemia isolates

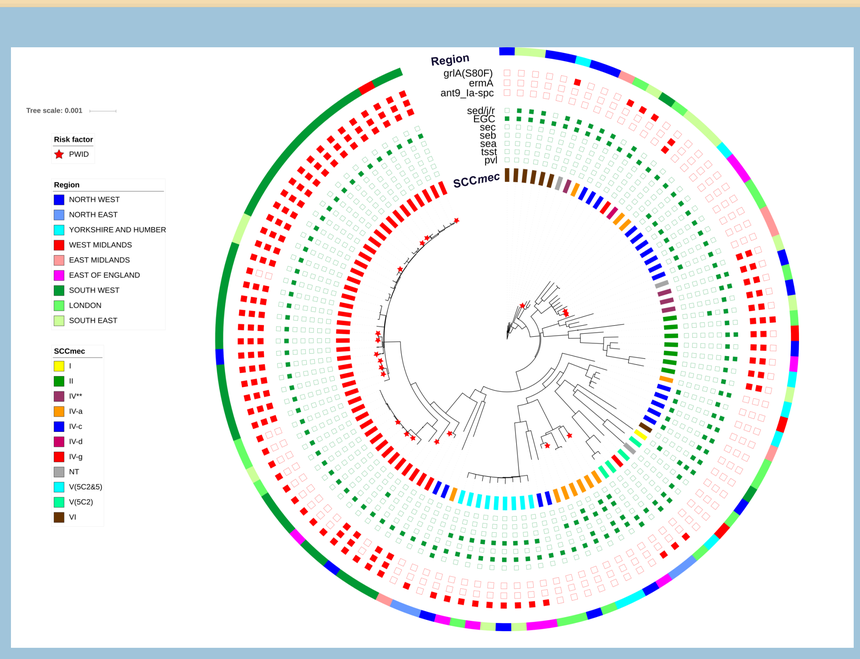

Figure 4. CC5 MRSA bacteraemia cases showing clonal expansion of CC5-IVg particularly among PWID ★

DISCUSSION

- This national initiative has afforded the most comprehensive study of MRSA bacteraemia in England with 76% cases captured across all 9 regions of England
- The integration of genomic and patient-level data has provided unprecedented insights into the complex and dynamic epidemiology of MRSA bacteraemia
- In the last decade, EMRSA-15 has declined from 85%[4] to 33%; similarly, EMRSA-16 has declined from 9%[4] to 1.2%
- CC5 has now emerged as the second most frequent clonal group and the PVL-MRSA rate has increased from 0[5] to 10.6%
- Detection of a CC5-SCC*mec*IVg clade in South West England has elicited public health investigations with a particular focus on the PWID community
- A genotypic MDR rate of 65.7% limits therapeutic options and raises public health concern across the one health landscape
- The increasing proportion of community onset cases (67%) suggests prevention efforts need to be strengthened in the community
- Integration of genomic and epidemiological data has afforded clear public health benefits in the detection of high risk clones, identification and expansion of successful clones and detection of linked cases
- In depth analyses of other clonal groups is ongoing to explore other possible clonal/epidemiological associations to inform the development of interventions aimed at reducing the incidence of MRSA bacteraemia

ACKNOWLEDGEMENTS

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