

Genomic investigation of Group B Streptococcus causing recurrent infections in infants in the United Kingdom

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Background

Group B Streptococcus (*Streptococcus agalactiae*, GBS) is a significant cause of invasive GBS (iGBS) disease in infants. Transmission routes and risk factors for early-onset GBS disease have been reported but what influences late-onset GBS disease, especially in nosocomial settings, are still not fully understood. A recurrent GBS infection can be described as a new episode of GBS that happens after the patient has successfully undergone treatment for an original GBS infection. A recent study (PMID: 34149682) reported that recurrent iGBS might be more common than initially thought. Genomic investigations of such cases are lacking, so we set out to characterise in depth genomic data for recurrent GBS isolates from the UK.

Material and Methods

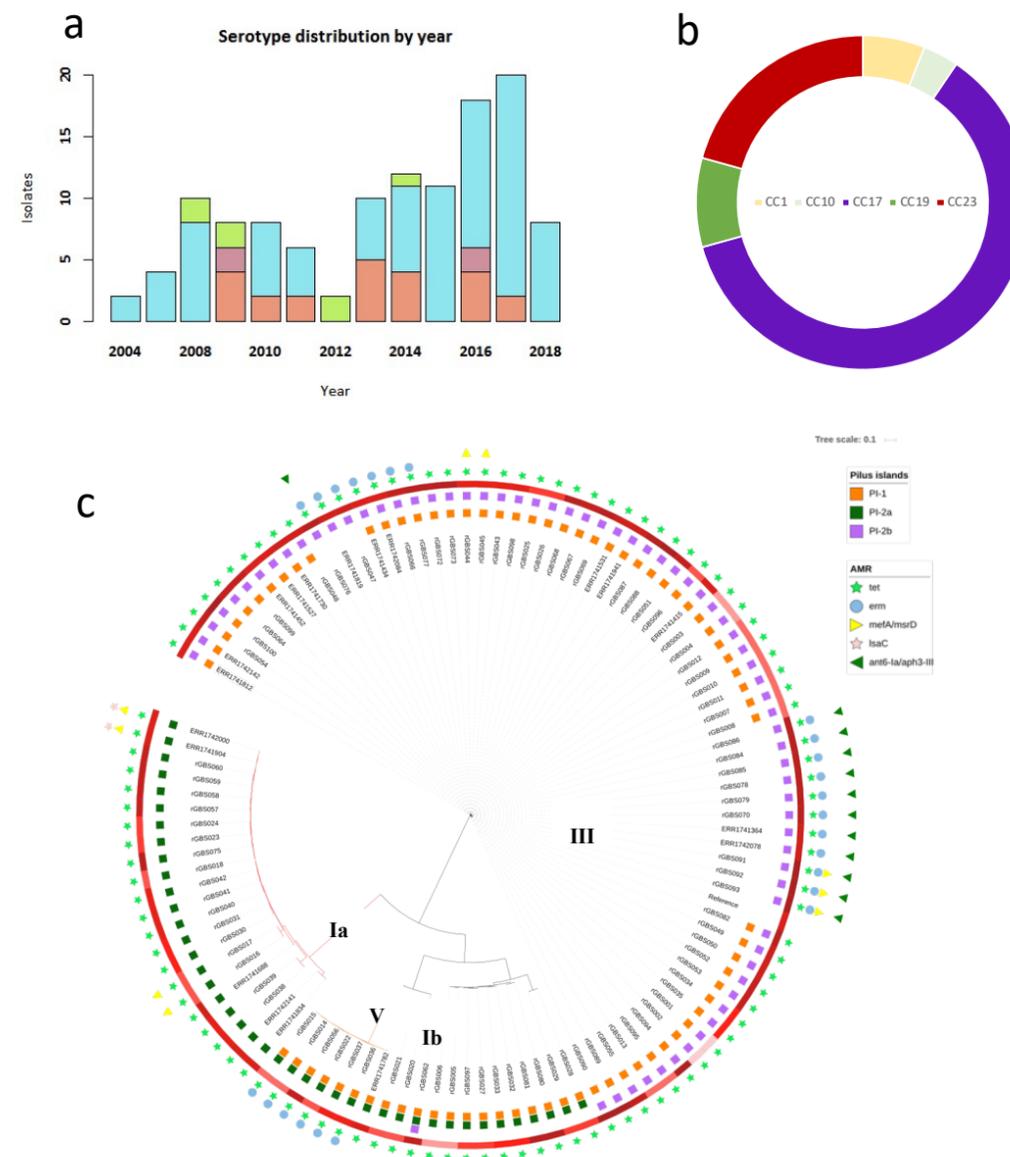
- A collection of 119 iGBS isolates from suspected recurrent infections in babies (< 1yrs) between 2004 and 2018.
- Whole genome sequencing of iGBS was undertaken using Illumina the HiSeq 2500 System (Illumina, US).
- GBS genomes underwent characterisation to determine serotype, multi-locus sequence type (MLST), antimicrobial resistance (AMR) genes and SNPs to infer relationships between the strains.

Isolates per patient	
2X isolates	49
3X isolates	7
Females	25
Males	31
Total	56
Isolation sites	
Blood culture	110
CSF	9

Table 1. Summary of sample types and numbers for recurrent iGBS cases.

Figure 1 (cont.) Panel a describes serotype distribution over the study period of 2004-2018. Panel b highlights isolate distribution based on clonal complex (CC). Panel c shows the phylogenetic tree constructed based on 21,270 core SNPs using the *S. agalactiae* strain COH1 as reference. Pilus and AMR gene combinations are indicated.

Figure 1. Characterisation of recurrent iGBS isolates based on serotype, genotype and phylogenetic relationship.



Results

- Four serotypes were found. Overall: serotype III (71%), Ia (20%), V (6%) and Ib (3%). Serotype III dominated each year as well (Figure 1a).
- Eleven STs were identified, with over half of the isolates belonging to ST17 (57%, n=63), followed by ST23 (14%, n=16). The most common clonal complexes were: CC17 (n=69; ST17, ST655 and ST1352) and CC23 (n=22; ST23, ST24, ST144 and ST1353)(Figure 1b).
- All iGBS isolates were carrying tetracycline resistance genes: *tetM* or *tetO*. Macrolide resistance genes (*mefA*, *msrD*, *ermB* or *ermT*) were detected in 27% of the isolates (n=30). 12 isolates also carried the *ant(6)-Ia* and *aph(3')-III* genes (Figure 1c).
- In 38 cases, at least two isolates from the same infant were within <7 SNPs difference, indicating persistence of the infecting strain or re-infection from a common source.
- Comparative analysis with other publicly available data has shown that recurrent iGBS isolates originate from the same genetic pool as other invasive GBS and carriage GBS isolates.

Conclusions and further work

In this study we have identified that serotype III ST17 strains were dominant among recurrent iGBS cases. We have identified that a third of isolates had antimicrobial resistance determinants to at least two antibiotic classes, highlighting the potential threat to treatment options. The integration of clinical data, detailed antibiotic treatment information as well as additional information on maternal GBS carriage would further elucidate why recurrent iGBS disease was observed.

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