

https://dspace.org/

Molecular characterization of invasive Streptococcus agalactiae in South Africa, 2019 – 2020

Ntozini, Buhle

2024
https://hdl.handle.net/10539/37639

Downloaded from a DSpace repository. https://dspace.org/

Name: Buhle Ntozini

Student no.: 2213934

Abstract

Background: Group B streptococcus (GBS) is a leading cause of neonatal meningitis and sepsis. Capsular polysaccharide and protein-based GBS vaccines are currently in development. Therefore, it is important to understand the serotype and antigen distribution of GBS to assess potential vaccine coverage. We aimed to use whole genome sequencing (WGS) and phenotypic methods to assess the serotype and antigen distribution, antimicrobial susceptibility patterns, and the phylogeny of invasive GBS isolates in South Africa (SA).

Methods: As part of national laboratory-based surveillance, 661 invasive GBS isolates cultured from normally sterile-site specimens (e.g. blood and cerebrospinal fluid) from patients of all ages, were collected from 2019-2020. Phenotypic identification was based on colony morphology and β-hemolysis. Serotyping was performed using latex agglutination. Antimicrobial susceptibility testing was based on disc diffusion and broth microdilution methods. Whole genome sequencing (WGS) was performed using the NextSeq 550 System and the 2 x 100-bp paired-end mode. WGS based prediction of serotypes, surface protein genes, and resistance gene detection was performed using a validated GBS bioinformatics pipeline developed by the US Centers for Disease Control and Prevention (CDC).

Results: A total of 658/661 isolates yielded good quality sequences from WGS and three isolates poor quality sequences. The isolates belonged to 6 major clonal complexes (CCs): CC1 (37/658, 5.6%), CC8/10 (69/658, 10.5%), CC17 (272/658, 41.3%), CC19 (45/658, 6.8%), CC23 (188/658, 28.6%) and CC24 (37/658, 5.6%). Five singletons (10/658, 1.5%) were identified. Excluding phenotypically and genotypically non-typeable isolates, concordance for serotyping using latex agglutination and WGS was 99.7% (647/649). Overall, 6 serotypes were detected: III (281/656, 42.8%), Ia (183/656, 27.9%), V (78/656, 11.9%), II (955/656, 8.4%), Ib (44/656, 6.7%), and IV (15/656, 2.3%). Three percent (20/658) of the isolates were non-susceptible to penicillin. Erythromycin and clindamycin resistance was detected in 16.1% (106/658) and 3.8% (25/657) of the isolates respectively. Majority (91.5%, 625/657) of the isolates were resistant to tetracycline. Fifty-five percent (11/20) of penicillin non-susceptible isolates had mutations in the PBP2x gene known to

confer resistance, while no PBP2x resistance mutation were detected in the remaining resistant isolates. *ermTR* (34.9%, 37/106) and *mefA/E* (29.2%, 31/106) resistance genes were the most common determinants of erythromycin resistance. Clindamycin resistance was mediated by the *erm* (*ermB, T,* and *TR*) genes. Tetracycline resistance was driven by the presence of the *tet* genes (*tetM, tetO, and tetL*), with *tetM* being the most common (95.8%, 599/625). Nearly all the isolates carried at least one of the 3 main pilus gene clusters (657/658, 99.8%), 1 of the 4 homologous alpha/Rib family determinants (656/658, 99.7%) and 1 of the serine-rich repeat (Srr) protein genes (626/658, 95.1%). The *hvgA* virulence gene was found exclusively in CC17 isolates.

Conclusion: Our results show that the majority of isolates circulating in SA belong to the 5 major GBS CCs (CC1, CC8/10, CC17, CC19, and CC23). This study suggests that vaccines currently under development should provide good coverage in our setting. We show that the GBS6 vaccine that targets serotypes Ia, Ib, II, III, IV, and V has the potential to cover 100% of invasive GBS disease in SA. A pilus protein-based vaccine has a potential coverage of 99.8% and the GBS-NN and the latch peptide vaccines have a potential coverage of 68.5% and 95.3% respectively. Beta-lactams remain appropriate for treatment and intrapartum antibiotic prophylaxis (IAP). However, detecting the emergence of non-susceptibility requires ongoing surveillance.