

Supplementary Materials for

A 15-year single-centre clinical and genomic analysis of late-onset Group B Streptococcus infection.

Table S1. Distribution of Clonal Complexes and Serotypes across Age Groups

	EOD (N=2)	LOD (N=48)	VLOD (N=20)	Older Children (N=10)	Adults (N=7)	Total Infants (N=70)	Total (N=87)
Serotypes							
Ia	2 (100%)	7 (15%)	6 (30%)	5 (50%)	1 (14%)	15 (21.4%)	21 (24.1%)
Ib	0 (0%)	2 (4%)	4 (20%)	1 (10%)	0 (0%)	6 (8.6%)	7 (8%)
II	0 (0%)	2 (4%)	0 (0%)	0 (0%)	1 (14%)	2 (2.9%)	3 (3.4%)
III	0 (0%)	36 (75%)	9 (45%)	1 (10%)	2 (29%)	45 (64.3%)	48 (55.2%)
IV	0 (0%)	1 (2%)	0 (0%)	1 (10%)	2 (29%)	1 (1.4%)	4 (4.6%)
V	0 (0%)	0 (0%)	1 (5%)	2 (20%)	1 (14%)	1 (1.4%)	4 (4.6%)
Clonal Complexes (CC)							
1	0 (0%)	0 (0%)	1 (5%)	2 (20%)	1 (14%)	1 (1.4%)	4 (4.6%)
12	0 (0%)	3 (6%)	4 (20%)	1 (10%)	0 (0%)	7 (10%)	8 (9.2%)
17	0 (0%)	31 (65%)	9 (45%)	1 (10%)	0 (0%)	40 (57.1%)	41 (47.1%)
19	0 (0%)	6 (12%)	0 (0%)	0 (0%)	3 (43%)	6 (8.6%)	9 (10.3%)
23	2 (100%)	7 (15%)	6 (30%)	5 (50%)	1 (14%)	15 (21.4%)	21 (24.1%)
459	0 (0%)	1 (2%)	0 (0%)	1 (10%)	2 (29%)	1 (1.4%)	4 (4.6%)

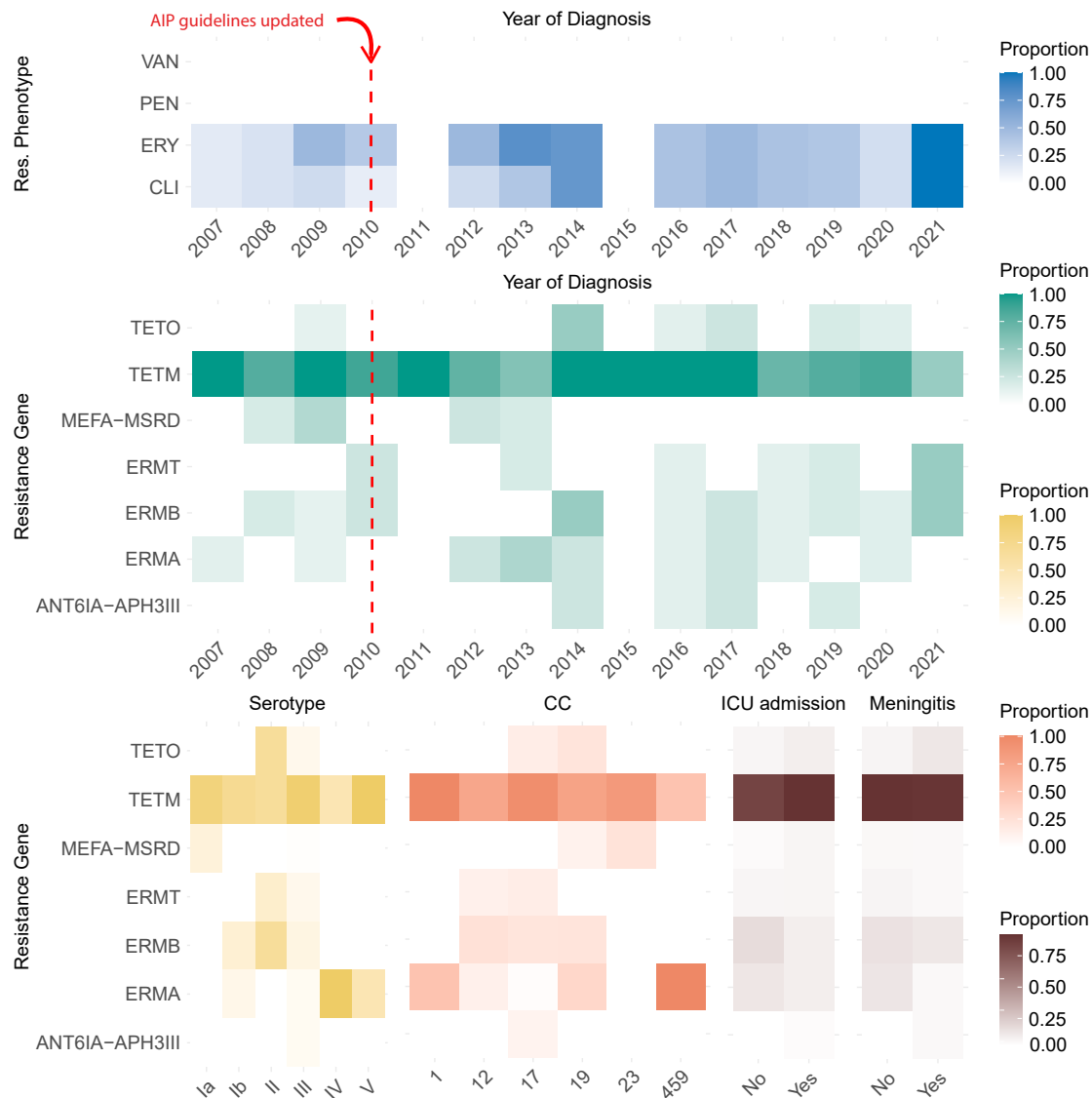


Figure S1. Distribution of Phenotypic Resistance Profiles and Genetic Resistance Markers Over Time, Serotypes, Clonal Complexes, and Clinical Outcomes (ICU admission & Meningitis). The top panel illustrates the distribution of phenotypic resistance profiles, as determined through antimicrobial susceptibility testing (AST), spanning the years 2007 to 2021. We have marked a dashed red line on the plot to indicate the revision that occurred in 2010 when the U.S. GBS AIP guidelines for pregnant individuals were updated to exclude erythromycin, due to increasing concerns about resistance. Notably, in 2010, the U.S. GBS AIP guidelines for pregnant individuals were revised, notably removing erythromycin due to concerns about resistance. These profiles include VAN (vancomycin), PEN (penicillin), ERY (erythromycin), and CLI (clindamycin). The middle and bottom panels illustrate the distribution of genetic resistance markers over time, along with their association with serotypes, clonal complexes, and clinical outcomes such as ICU admission and meningitis. The resistance markers identified in our dataset include ant(6)-Ia-aph(3')-III, which confers resistance to aminoglycosides; ermA, ermB, and ermT are associated with the MLSB phenotype, conferring resistance to macrolides (such as erythromycin), lincosamides (such as clindamycin), and streptogramin B antibiotics; mef(A)-msr(D) confers resistance to macrolides; and tetM and tetO confer resistance to tetracyclines.

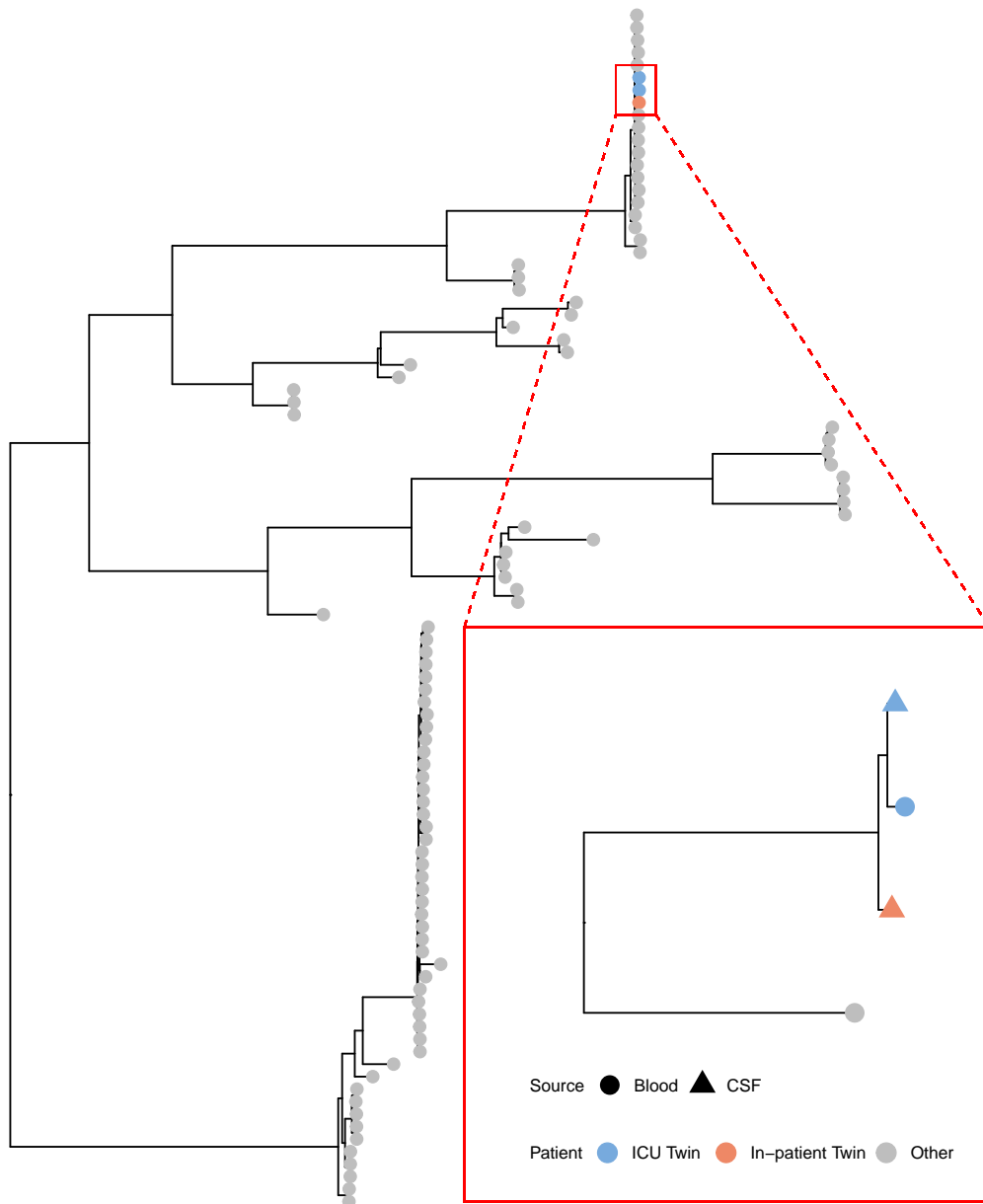


Figure S2. Distribution of VLOD Twins in Boston Children's Hospital (BCH) Group B Streptococcus (GBS) Phylogeny. Both twins were infected with CC23/cpsIa GBS isolates, which are clustered together in the phylogenetic analysis. One twin had GBS isolates from both blood (indicated by a circle) and cerebrospinal fluid (CSF, indicated by a triangle) and was treated in the ICU (highlighted with blue tips). The other twin had GBS isolated only from the CSF and received treatment in the inpatient pediatric unit (highlighted with orange tips).

Table S2. Distribution of Clonal complexes (CCs) and Sequence Types (STs) by Age group

	EOD (N=2)	LOD (N=48)	VLOD (N=20)	Older Children (N=10)	Adults (N=7)	Total (N=87)
CC1						
ST1	0 (0%)	0 (0%)	1 (5%)	2 (20%)	1 (14%)	4
CC12						
ST10	0 (0%)	1 (2%)	1 (5%)	1 (0%)	0 (0%)	3
ST8	0 (0%)	1 (2%)	3 (15%)	0 (0%)	0 (0%)	4
NF	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1
Total	0 (0%)	3 (6%)	4 (20%)	1 (10%)	0 (0%)	8
CC17						
ST109	0 (0%)	1 (2%)	1 (5%)	0 (0%)	0 (0%)	2
ST147	0 (0%)	2 (4%)	1 (5%)	0 (0%)	0 (0%)	3
ST17	0 (0%)	26 (54%)	5 (25%)	1 (10%)	0 (0%)	32
ST17*	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1
ST31	0 (0%)	0 (0%)	2 (10%)	0 (0%)	0 (0%)	2
ST860	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1
Total	0 (0%)	31 (65%)	9 (45%)	1 (10%)	0 (0%)	41
CC19						
ST19	0 (0%)	3 (6%)	0 (0%)	0 (0%)	2 (29%)	5
ST28	0 (0%)	1 (2%)	0 (0%)	0 (0%)	1 (14%)	2
ST335	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1
ST1563*	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1
Total	0 (0%)	6 (12%)	0 (0%)	0 (0%)	3 (43%)	9
CC23						
ST174	0 (0%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	5
ST23	2 (100%)	6 (12%)	5 (25%)	4 (40%)	0 (0%)	17
ST88	0 (0%)	0 (0%)	0 (0%)	1 (10%)	1 (14%)	1
ST88*	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1
Total	2 (100%)	7 (15%)	6 (30%)	5 (50%)	1 (14%)	9
CC459						
ST459	0 (0%)	1 (2%)	0 (0%)	1 (10%)	2 (29%)	4
Others						
NF	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1

* indicates the best scoring allele has ≥ 1 mismatch (SNP or indel).

EOD: <7 days, LOD:7-89 days, VLOD:90-365 days, Older Children:1-17 years, Adults: ≥ 18 years

Table S3. Allelic profiles of different sequence types (STs) in our study.

ST	N (%)	adhP	pheS	atr	glnA	sdhA	glcK	tkr	mismatches
Known STs									
17	32 (37%)	2	1	1	2	1	1	1	
23	17 (20%)	5	4	6	3	2	1	3	
19	5 (6%)	1	1	3	2	2	2	2	
1	4 (5%)	1	1	2	1	1	2	2	
459	4 (5%)	1	1	3	1	41	12	2	
8	4 (5%)	4	1	4	1	3	3	2	
10	3 (3%)	9	1	4	2	3	3	2	
1470	3 (3%)	2	1	188	2	1	1	1	
109	2 (2%)	2	1	1	10	1	1	1	
28	2 (2%)	1	1	3	5	2	2	2	
31	2 (2%)	2	1	1	6	1	1	1	
88	2 (2%)	5	10	6	3	2	1	3	
1747	1 (1%)	5	141	6	3	2	1	3	
335	1 (1%)	1	1	43	2	2	2	2	
860	1 (1%)	157	1	1	2	1	1	1	
Known STs with mismatches									
1563*	1 (1%)	1	1	202*	2	2	2	2	atr_202/1snp
17*	1 (1%)	2	1	1*	2	1	1	1	atr_1/1snp
88*	1 (1%)	5	10	6	3	2	1*	3	glcK_1/1snp
New ST profile									
NF	1 (1%)	4	1	4	4	3	3	2	

Table S4. Distribution of vaccine candidate targets and other immunogenic proteins across age groups in our study.

	EOD (N=2)	LOD (N=48)	VLOD (N=20)	Older Children (N=10)	Adults (N=7)	Total Infants (N=70)	Total (N=87)
Capsular polysaccharide vaccine							
Trivalent*	2 (100%)	45 (94%)	19 (95%)	7 (70%)	3 (43%)	66 (94%)	76 (87%)
Hexavalent*	2 (100%)	48 (100%)	20 (100%)	10 (100%)	7 (100%)	70 (100%)	87 (100%)
Protein subunit vaccine							
RIB	0 (0%)	37 (77%)	9 (45%)	1 (10%)	3 (43%)	46 (66%)	50 (57%)
ALPHA C	0 (0%)	3 (6%)	4 (20%)	1 (10%)	0 (0%)	7 (10%)	8 (9%)
ALP1	2 (100%)	7 (15%)	6 (30%)	5 (50%)	2 (29%)	15 (21%)	22 (25%)
ALP23	0 (0%)	1 (2%)	1 (5%)	3 (30%)	2 (29%)	2 (3%)	7 (8%)
GBS-NN2*	2 (100%)	48 (100%)	20 (100%)	10 (100%)	7 (100%)	70 (100%)	87 (100%)
Other Immunogenic Proteins							
Pilus proteins							
PI1	0 (0%)	36 (75%)	13 (65%)	6 (60%)	6 (86%)	49 (70%)	61 (70%)
PI2a1	2 (100%)	8 (17%)	11 (55%)	7 (70%)	1 (14%)	21 (30%)	29 (33%)
PI2a2	0 (0%)	6 (12%)	0 (0%)	0 (0%)	3 (43%)	6 (9%)	9 (10%)
PI2b	0 (0%)	30 (62%)	8 (40%)	1 (10%)	0 (0%)	38 (54%)	39 (45%)
PI1+PI2a1+ PI2a2+PI2b	2 (100%)	48 (100%)	20 (100%)	10 (100%)	7 (100%)	70 (100%)	87 (100%)
Sip proteins							
Sip.1a	0 (0%)	7 (15%)	1 (5%)	3 (30%)	6 (86%)	8 (11%)	17 (20%)
Sip.3a	2 (100%)	41 (85%)	19 (95%)	7 (70%)	1 (14%)	62 (89%)	70 (80%)
Sip	2 (100%)	48 (100%)	20 (100%)	10 (100%)	7 (100%)	70 (100%)	87 (100%)
Others							
C5a (scpB)	20 (100%)	47 (98%)	19 (95%)	8 (80%)	6 (86%)	68 (97%)	82 (94%)
Lmb	20 (100%)	47 (98%)	20 (100%)	10 (100%)	7 (100%)	69 (99%)	86 (99%)
FbsB	20 (100%)	38 (79%)	15 (75%)	6 (60%)	1 (14%)	55 (79%)	62 (71%)
Other Virulence Factors							
SRR proteins							
SRR1	2 (100%)	16 (33%)	11 (55%)	9 (90%)	6 (86%)	29 (41%)	44 (51%)
SRR2	0 (0%)	31 (65%)	9 (45%)	1 (10%)	0 (0%)	40 (57%)	41 (47%)
SRR1+SRR2	2 (100%)	47 (98%)	20 (100%)	10 (100%)	6 (86%)	69 (99%)	85 (98%)

EOD:<7 days, LOD:7-89 days, VLOD:90-365 days, Older Children:1-17 years, Adults:≥ 18 years

*Trivalent: covers serotypes Ia/Ib/III

*Hexavalent/GBS6: covers serotypes Ia/Ib/II/III/IV/V

*GBS-NN2: covers ALP proteins RIB + AlphaC + Alp1 + Alp2/3

Table S5. Genetic Resistance Markers Across Different Clonal Complexes (CCs)

	CC1 (N=4)	CC12 (N=8)	CC17 (N=41)	CC19 (N=9)	CC23 (N=21)	CC459 (N=4)	Total (N=87)
Aminoglycosides Resistance							
ANT6_IA	0 (0%)	0 (0%)	4 (10%)	0 (0%)	0 (0%)	0 (0%)	4 (5%)
APH3_III	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total	0 (0%)	0 (0%)	4 (10%)	0 (0%)	0 (0%)	0 (0%)	4 (5%)
Tetracyclines Resistance							
TETM	4 (100%)	6 (75%)	39 (95%)	7 (78%)	18 (86%)	2 (50%)	76 (87%)
TETO	0 (0%)	0 (0%)	6 (15%)	2 (22%)	0 (0%)	0 (0%)	8 (9%)
Total	4 (100%)	6 (75%)	40 (98%)	8 (89%)	18 (86%)	2 (50%)	78 (90%)
MLSB Resistance							
ERMA	2 (50%)	1 (12%)	1 (2%)	3 (33%)	0 (0%)	4 (100%)	11 (13%)
ERMB	0 (0%)	2 (25%)	9 (22%)	2 (22%)	0 (0%)	0 (0%)	13 (15%)
ERMT	0 (0%)	1 (12%)	6 (15%)	0 (0%)	0 (0%)	0 (0%)	7 (8%)
Total	2 (50%)	4 (50%)	16 (39%)	5 (56%)	0 (0%)	4 (100%)	31 (36%)
M type Resistance							
MEFA	0 (0%)	0 (0%)	0 (0%)	1 (11%)	5 (24%)	0 (0%)	6 (7%)
MSRD	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total	0 (0%)	0 (0%)	0 (0%)	1 (11%)	5 (24%)	0 (0%)	6 (7%)
Fluoroquinolone Resistance							
GYRA	0 (0%)	2 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (2%)
PARC	0 (0%)	2 (25%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	3 (3%)
Total	0 (0%)	4 (50%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	5 (6%)

Table S6. Molecular Risk Factors of Age of Disease Onset (Infants vs Older Patients)

	Infants (n=70)	Older Patients (n=17)	OR	Crude (LR) (95% CI)	P-value	OR	Adjusted (LMM) (95% CI)	P-value
ALP protein family								
ALP1	15 (21.4%)	7 (41.2%)	0.39	(0.13 - 1.20)	0.1000	1.02	1.02 (0.71; 1.45)	0.9210
ALP23	2 (2.9%)	5 (29.4%)	0.07	(0.01 - 0.41)	0.0030	0.71	0.71 (0.49; 1.02)	0.0636
ALPHA	7 (10%)	1 (5.9%)	1.78	(0.20 - 15.51)	0.6030	1.45	1.45 (0.93; 2.26)	0.1070
RIB	46 (65.7%)	4 (23.5%)	6.23	(1.83 - 21.20)	0.0030	1.12	1.12 (0.72; 1.75)	0.6150
Pilus Islands								
PII	49 (70%)	12 (70.6%)	0.97	(0.30 - 3.11)	0.9620	0.96	0.96 (0.76; 1.22)	0.7330
PI2A1	21 (30%)	8 (47.1%)	0.48	(0.16 - 1.42)	0.1860	1.16	1.16 (0.85; 1.6)	0.3570
PI2A2	6 (8.6%)	3 (17.6%)	0.44	(0.10 - 1.96)	0.2810	0.92	0.92 (0.57; 1.49)	0.7270
PI2A	27 (38.6%)	11 (64.7%)	0.34	(0.11 - 1.03)	0.0570	1.11	1.11 (0.81; 1.52)	0.5010
PI2B	38 (54.3%)	1 (5.9%)	19.00	(2.39 - 151.22)	0.0050	1.12	1.12 (0.77; 1.63)	0.5580
SRR Variants								
SRR1	29 (41.4%)	15 (88.2%)	0.09	(0.02 - 0.44)	0.0030	0.97	0.97 (0.63; 1.51)	0.9060
SRR2	40 (57.1%)	1 (5.9%)	21.33	(2.68 - 169.91)	0.0040	1.36	1.36 (0.77; 2.39)	0.2900
Sip Protein Variants								
Sip.1a	8 (11.4%)	9 (52.9%)	0.11	(0.03 - 0.38)	0.0000	0.72	0.72 (0.49; 1.05)	0.0931
Sip.3a	62 (88.6%)	8 (47.1%)	8.72	(2.62 - 29.06)	0.0000	1.39	1.39 (0.95; 2.03)	0.0931
Other Virulence factors								
HVGA	40 (57.1%)	1 (5.9%)	21.33	(2.68 - 169.91)	0.0040	1.36	1.36 (0.77; 2.39)	0.2900
lmb	69 (98.6%)	17 (100%)	0.00	(0.00 - Inf)	0.9920	0.78	0.78 (0.38; 1.6)	0.4990
scpB	68 (97.1%)	14 (82.4%)	7.29	(1.11 - 47.72)	0.0380	1.08	1.08 (0.7; 1.68)	0.7180
hylB	65 (92.9%)	15 (88.2%)	1.73	(0.31 - 9.81)	0.5340	0.90	0.9 (0.54; 1.48)	0.6660
fbsB	55 (78.6%)	7 (41.2%)	5.24	(1.71 - 16.09)	0.0040	1.09	1.09 (0.69; 1.7)	0.7200

Table S7. Molecular Risk Factors for ICU Admission among Infants

	ICU (n=31)	Other (n=39)	OR	Crude (LR) (95% CI)	P-value	OR	Adjusted (LMM) (95% CI)	P-value
ALP protein family								
ALP1	10 (32.3%)	5 (12.8%)	3.24	(0.97 - 10.79)	0.0560	1.27	(0.86; 1.86)	0.2330
ALP23	0 (0%)	2 (5.1%)	0.00	(0.00 - Inf)	0.9920	0.60	(0.29; 1.2)	0.1540
ALPHA	4 (12.9%)	3 (7.7%)	1.78	(0.37 - 8.61)	0.4750	1.17	(0.74; 1.84)	0.5110
RIB	17 (54.8%)	29 (74.4%)	0.42	(0.15 - 1.15)	0.0910	0.85	(0.6; 1.21)	0.3770
Pilus Islands								
PI1	18 (58.1%)	31 (79.5%)	0.36	(0.12 - 1.03)	0.0560	0.82	(0.61; 1.1)	0.1830
PI2A1	14 (45.2%)	7 (17.9%)	3.76	(1.28 - 11.10)	0.0160	1.40	(1; 1.95)	0.0571
PI2A2	3 (9.7%)	3 (7.7%)	1.29	(0.24 - 6.86)	0.7690	1.02	(0.63; 1.63)	0.9500
PI2A	17 (54.8%)	10 (25.6%)	3.52	(1.28 - 9.65)	0.0140	1.40	(1; 1.96)	0.0517
PI2B	13 (41.9%)	25 (64.1%)	0.40	(0.15 - 1.06)	0.0670	0.83	(0.59; 1.16)	0.2850
SRR Variants								
SRR1	17 (54.8%)	12 (30.8%)	2.73	(1.02 - 7.29)	0.0450	1.28	(0.89; 1.82)	0.1870
SRR2	14 (45.2%)	26 (66.7%)	0.41	(0.16 - 1.09)	0.0730	0.83	(0.57; 1.2)	0.3290
Sip Protein Variants								
Sip.1a	3 (9.7%)	5 (12.8%)	0.73	(0.16 - 3.32)	0.6820	0.87	(0.57; 1.31)	0.4990
Sip.3a	28 (90.3%)	34 (87.2%)	1.37	(0.30 - 6.25)	0.6820	1.15	(0.76; 1.75)	0.4990
Other Virulence factors								
HVGA	14 (45.2%)	26 (66.7%)	0.41	(0.16 - 1.09)	0.0730	0.83	(0.57; 1.2)	0.3290
lmb	30 (96.8%)	39 (100%)	0.00	(0.00 - Inf)	0.9910	0.57	(0.21; 1.54)	0.2740
scpB	30 (96.8%)	38 (97.4%)	0.79	(0.05 - 13.15)	0.8690	0.94	(0.45; 1.95)	0.8740
hylB	28 (90.3%)	37 (94.9%)	0.50	(0.08 - 3.23)	0.4700	0.86	(0.52; 1.43)	0.5640
fbsB	24 (77.4%)	31 (79.5%)	0.88	(0.28 - 2.78)	0.8340	1.01	(0.7; 1.46)	0.9450

Table S8. Molecular Risk factors for Meningitis among Infants

	Meningitis (n=13)	No Meningitis (n=57)	OR	Crude (LR) (95% CI)	P-value	OR	Adjusted (LMM) (95% CI)	P-value
ALP protein family								
ALP1	4 (30.8%)	11 (19.3%)	1.86	(0.48 - 7.16)	0.3680	1.11	(0.89; 1.39)	0.3700
ALP23	0 (0%)	2 (3.5%)	0.00	(0.00 - Inf)	0.9930	0.83	(0.48; 1.44)	0.5000
ALPHA	1 (7.7%)	6 (10.5%)	0.71	(0.08 - 6.45)	0.7600	0.95	(0.7; 1.3)	0.7630
RIB	8 (61.5%)	38 (66.7%)	0.80	(0.23 - 2.78)	0.7260	0.97	(0.8; 1.17)	0.7300
Pilus Islands								
PI1	7 (53.8%)	42 (73.7%)	0.42	(0.12 - 1.44)	0.1660	0.87	(0.71; 1.06)	0.1640
PI2A1	5 (38.5%)	16 (28.1%)	1.60	(0.46 - 5.63)	0.4630	1.08	(0.88; 1.32)	0.4680
PI2A2	2 (15.4%)	4 (7%)	2.41	(0.39 - 14.83)	0.3430	1.17	(0.85; 1.63)	0.3380
PI2A	7 (53.8%)	20 (35.1%)	2.16	(0.64 - 7.30)	0.2160	1.13	(0.93; 1.36)	0.2160
PI2B	4 (30.8%)	34 (59.6%)	0.30	(0.08 - 1.09)	0.0680	0.84	(0.7; 1)	0.0606
SRR Variants								
SRR1	6 (46.2%)	23 (40.4%)	1.27	(0.38 - 4.26)	0.7020	1.04	(0.86; 1.25)	0.7060
SRR2	6 (46.2%)	34 (59.6%)	0.58	(0.17 - 1.95)	0.3780	0.92	(0.76; 1.11)	0.3820
Sip Protein Variants								
Sip.1a	2 (15.4%)	6 (10.5%)	1.55	(0.27 - 8.70)	0.6210	1.08	(0.8; 1.44)	0.6250
Sip.3a	11 (84.6%)	51 (89.5%)	0.65	(0.11 - 3.64)	0.6210	0.93	(0.7; 1.24)	0.6250
Other Virulence factors								
HVGA	6 (46.2%)	34 (59.6%)	0.58	(0.17 - 1.95)	0.3780	0.92	(0.76; 1.11)	0.3820
lmb	13 (100%)	56 (98.2%)	Inf	(0.00 - Inf)	0.9920	1.21	(0.55; 2.63)	0.6360
scpB	13 (100%)	55 (96.5%)	Inf	(0.00 - Inf)	0.9930	1.21	(0.7; 2.1)	0.5000
hylB	12 (92.3%)	53 (93%)	0.91	(0.09 - 8.85)	0.9320	0.98	(0.69; 1.41)	0.9330
fbsB	10 (76.9%)	45 (78.9%)	0.89	(0.21 - 3.75)	0.8730	0.98	(0.78; 1.23)	0.8750

Table S9. Molecular Risk Factors for Neutropenia among Infants

	Neutropenia (n=13)	No Neutropenia (n=55)	OR	Crude (LR) (95% CI)	P-value	OR	Adjusted (LMM) (95% CI)	P-value
ALP protein family								
ALP1	1 (7.7%)	14 (25.5%)	0.24	(0.03 - 2.05)	0.1940	0.85	(0.68; 1.07)	0.1700
ALP23	0 (0%)	2 (3.6%)	0.00	(0.00 - Inf)	0.9930	0.82	(0.47; 1.44)	0.4930
ALPHA	2 (15.4%)	5 (9.1%)	1.82	(0.31 - 10.62)	0.5070	1.11	(0.81; 1.52)	0.5090
RIB	10 (76.9%)	34 (61.8%)	2.06	(0.51 - 8.35)	0.3120	1.11	(0.91; 1.35)	0.3130
Pilus Islands								
PI1	11 (84.6%)	36 (65.5%)	2.90	(0.58 - 14.46)	0.1930	1.15	(0.94; 1.41)	0.1840
PI2A1	3 (23.1%)	18 (32.7%)	0.62	(0.15 - 2.52)	0.5010	0.93	(0.76; 1.14)	0.5050
PI2A2	3 (23.1%)	3 (5.5%)	5.20	(0.91 - 29.55)	0.0630	1.40	(1.02; 1.94)	0.0447
PI2A	6 (46.2%)	21 (38.2%)	1.39	(0.41 - 4.69)	0.5980	1.05	(0.87; 1.28)	0.6040
PI2B	5 (38.5%)	31 (56.4%)	0.48	(0.14 - 1.67)	0.2500	0.89	(0.74; 1.08)	0.2510
SRR Variants								
SRR1	5 (38.5%)	24 (43.6%)	0.81	(0.23 - 2.78)	0.7350	0.97	(0.8; 1.17)	0.7390
SRR2	7 (53.8%)	31 (56.4%)	0.90	(0.27 - 3.04)	0.8690	0.98	(0.81; 1.19)	0.8720
Sip Protein Variants								
Sip.1a	3 (23.1%)	5 (9.1%)	3.00	(0.62 - 14.63)	0.1740	1.23	(0.92; 1.65)	0.1640
Sip.3a	10 (76.9%)	50 (90.9%)	0.33	(0.07 - 1.63)	0.1740	0.81	(0.61; 1.09)	0.1640
Other Virulence factors								
HVGA	7 (53.8%)	31 (56.4%)	0.90	(0.27 - 3.04)	0.8690	0.98	(0.81; 1.19)	0.8720
lmb	13 (100%)	54 (98.2%)	Inf	(0.00 - Inf)	0.9920	1.21	(0.55; 2.66)	0.6300
scpB	13 (100%)	53 (96.4%)	Inf	(0.00 - Inf)	0.9930	1.22	(0.7; 2.13)	0.4930
hylB	11 (84.6%)	52 (94.5%)	0.32	(0.05 - 2.13)	0.2370	0.80	(0.56; 1.14)	0.2230
fbsB	8 (61.5%)	45 (81.8%)	0.36	(0.10 - 1.32)	0.1220	0.83	(0.67; 1.04)	0.1160

Table S10. Molecular Risk Factors for Leukopenia among Infants

	Leukopenia (n=16)	No Leukopenia (n=52)	OR	Crude (LR) (95% CI)	P-value	OR	Adjusted (LMM) (95% CI)	P-value
ALP protein family								
ALP1	3 (18.8%)	12 (23.1%)	0.77	(0.19 - 3.16)	0.7160	0.89	(0.64; 1.22)	0.4680
ALP23	1 (6.2%)	1 (1.9%)	3.40	(0.20 - 57.67)	0.3970	1.24	(0.68; 2.29)	0.4850
ALPHA	3 (18.8%)	4 (7.7%)	2.77	(0.55 - 13.96)	0.2170	1.16	(0.79; 1.71)	0.4440
RIB	9 (56.2%)	35 (67.3%)	0.62	(0.20 - 1.96)	0.4200	0.96	(0.72; 1.29)	0.7950
Pilus Islands								
PI1	12 (75%)	35 (67.3%)	1.46	(0.41 - 5.20)	0.5620	1.09	(0.85; 1.41)	0.4990
PI2A1	7 (43.8%)	14 (26.9%)	2.11	(0.66 - 6.75)	0.2080	1.16	(0.87; 1.54)	0.3250
PI2A2	3 (18.8%)	3 (5.8%)	3.77	(0.68 - 20.91)	0.1290	1.32	(0.89; 1.96)	0.1700
PI2A	10 (62.5%)	17 (32.7%)	3.43	(1.07 - 11.01)	0.0380	1.33	(1.01; 1.76)	0.0474
PI2B	5 (31.2%)	31 (59.6%)	0.31	(0.09 - 1.02)	0.0530	0.78	(0.59; 1.03)	0.0848
SRR Variants								
SRR1	9 (56.2%)	20 (38.5%)	2.06	(0.66 - 6.40)	0.2130	1.11	(0.82; 1.5)	0.4920
SRR2	6 (37.5%)	32 (61.5%)	0.37	(0.12 - 1.19)	0.0960	0.81	(0.6; 1.1)	0.1870
Sip Protein Variants								
Sip.1a	4 (25%)	4 (7.7%)	4.00	(0.87 - 18.35)	0.0750	1.32	(0.93; 1.86)	0.1240
Sip.3a	12 (75%)	48 (92.3%)	0.25	(0.05 - 1.15)	0.0750	0.76	(0.54; 1.07)	0.1240
Other Virulence factors								
HVGA	6 (37.5%)	32 (61.5%)	0.37	(0.12 - 1.19)	0.0960	0.81	(0.6; 1.1)	0.1870
lmb	15 (93.8%)	52 (100%)	0.00	(0.00 - Inf)	0.9910	0.49	(0.21; 1.14)	0.1040
scpB	14 (87.5%)	52 (100%)	0.00	(0.00 - Inf)	0.9920	0.47	(0.26; 0.86)	0.0170
hylB	14 (87.5%)	49 (94.2%)	0.43	(0.07 - 2.82)	0.3780	0.87	(0.57; 1.34)	0.5440
fbsB	9 (56.2%)	44 (84.6%)	0.23	(0.07 - 0.81)	0.0220	0.74	(0.55; 1)	0.0524

Table S11. Molecular Risk Factors for Leukocytosis among Infants

	Leukocytosis (n=24)	No Leukocytosis (n=44)	OR	Crude (LR) (95% CI)	P-value	OR	Adjusted (LMM) (95% CI)	P-value
ALP protein family								
ALP1	5 (20.8%)	10 (22.7%)	0.89	(0.27 - 3.00)	0.8570	0.98	(0.74; 1.29)	0.8600
ALP23	1 (4.2%)	1 (2.3%)	1.87	(0.11 - 31.29)	0.6630	1.16	(0.59; 2.3)	0.6640
ALPHA	2 (8.3%)	5 (11.4%)	0.71	(0.13 - 3.96)	0.6950	0.93	(0.64; 1.35)	0.7000
RIB	16 (66.7%)	28 (63.6%)	1.14	(0.40 - 3.26)	0.8030	1.03	(0.81; 1.31)	0.8060
Pilus Islands								
PI1	19 (79.2%)	28 (63.6%)	2.17	(0.68 - 6.93)	0.1910	1.18	(0.92; 1.51)	0.1910
PI2A1	6 (25%)	15 (34.1%)	0.64	(0.21 - 1.96)	0.4400	0.91	(0.71; 1.16)	0.4460
PI2A2	1 (4.2%)	5 (11.4%)	0.34	(0.04 - 3.09)	0.3370	0.82	(0.54; 1.22)	0.3250
PI2A	7 (29.2%)	20 (45.5%)	0.49	(0.17 - 1.43)	0.1930	0.86	(0.68; 1.08)	0.1950
PI2B	15 (62.5%)	21 (47.7%)	1.83	(0.66 - 5.04)	0.2460	1.14	(0.91; 1.44)	0.2500
SRR Variants								
SRR1	9 (37.5%)	20 (45.5%)	0.72	(0.26 - 1.99)	0.5270	0.93	(0.74; 1.17)	0.5330
SRR2	15 (62.5%)	23 (52.3%)	1.52	(0.55 - 4.20)	0.4180	1.10	(0.87; 1.39)	0.4250
Sip Protein Variants								
Sip.1a	2 (8.3%)	6 (13.6%)	0.58	(0.11 - 3.10)	0.5210	0.89	(0.62; 1.27)	0.5240
Sip.3a	22 (91.7%)	38 (86.4%)	1.74	(0.32 - 9.36)	0.5210	1.12	(0.79; 1.61)	0.5240
Other Virulence factors								
HVGA	15 (62.5%)	23 (52.3%)	1.52	(0.55 - 4.20)	0.4180	1.10	(0.87; 1.39)	0.4250
lmb	24 (100%)	43 (97.7%)	Inf	(0.00 - Inf)	0.9920	1.43	(0.55; 3.72)	0.4640
scpB	24 (100%)	42 (95.5%)	Inf	(0.00 - Inf)	0.9920	1.44	(0.73; 2.83)	0.2960
hylB	23 (95.8%)	40 (90.9%)	2.30	(0.24 - 21.83)	0.4680	1.18	(0.76; 1.83)	0.4650
fbsB	20 (83.3%)	33 (75%)	1.67	(0.47 - 5.95)	0.4310	1.12	(0.85; 1.47)	0.4360

Table S12. Molecular Risk Factors of Age of Disease Onset among Infants (LOD vs VL0D)

	LOD (n=48)	VL0D (n=20)	OR	Crude (LR) (95% CI)	P-value	OR	Adjusted (LMM) (95% CI)	P-value
ALP protein family								
ALP1	6 (30%)	7 (14.6%)	0.40	(0.11 - 1.39)	0.1480	0.87	(0.56; 1.33)	0.5140
ALP23	1 (5%)	1 (2.1%)	0.40	(0.02 - 6.80)	0.5290	0.89	(0.46; 1.74)	0.7390
ALPHA	4 (20%)	3 (6.2%)	0.27	(0.05 - 1.32)	0.1060	0.77	(0.48; 1.24)	0.2850
RIB	9 (45%)	37 (77.1%)	4.11	(1.36 - 12.46)	0.0120	1.42	(0.96; 2.11)	0.0849
Pilus Islands								
PI1	13 (65%)	36 (75%)	1.62	(0.52 - 4.99)	0.4040	1.04	(0.77; 1.4)	0.7950
PI2A1	11 (55%)	8 (16.7%)	0.16	(0.05 - 0.52)	0.0020	0.60	(0.42; 0.85)	0.0058
PI2A2	0 (0%)	6 (12.5%)	Inf	(0.00 - Inf)	0.9920	1.47	(0.91; 2.38)	0.1190
PI2A	11 (55%)	14 (29.2%)	0.34	(0.11 - 0.99)	0.0480	0.74	(0.51; 1.08)	0.1260
PI2B	8 (40%)	30 (62.5%)	2.50	(0.86 - 7.28)	0.0930	1.19	(0.82; 1.74)	0.3550
SRR Variants								
SRR1	11 (55%)	16 (33.3%)	0.41	(0.14 - 1.19)	0.1000	0.85	(0.56; 1.3)	0.4660
SRR2	9 (45%)	31 (64.6%)	2.23	(0.77 - 6.44)	0.1390	1.12	(0.71; 1.75)	0.6290
Sip Protein Variants								
Sip.1a	1 (5%)	7 (14.6%)	3.24	(0.37 - 28.26)	0.2870	1.30	(0.86; 1.98)	0.2210
Sip.3a	19 (95%)	41 (85.4%)	0.31	(0.04 - 2.69)	0.2870	0.77	(0.5; 1.17)	0.2210
Other Virulence factors								
HVGA	9 (45%)	31 (64.6%)	2.23	(0.77 - 6.44)	0.1390	1.12	(0.71; 1.75)	0.6290
lmb	20 (100%)	47 (97.9%)	0.00	(0.00 - Inf)	0.9920	0.60	(0.24; 1.49)	0.2770
scpB	19 (95%)	47 (97.9%)	2.47	(0.15 - 41.61)	0.5290	1.05	(0.53; 2.07)	0.8950
hylB	20 (100%)	43 (89.6%)	0.00	(0.00 - Inf)	0.9920	0.71	(0.42; 1.18)	0.1880
fbsB	15 (75%)	38 (79.2%)	1.27	(0.37 - 4.33)	0.7060	0.95	(0.63; 1.42)	0.7980

Table S13. Molecular Risk Factors of Age of Disease Onset among Infants (continuous)

	Adjusted for Pop. Structure (LMM)		
	Absolute increase in probability (β)	Standard Error	P-value
ALP protein family			
ALP1	-13.50	38.60	0.7270
ALP23	67.90	48.40	0.1660
ALPHA	32.70	41.30	0.4310
RIB	-57.30	38.20	0.1380
Pilus Islands			
PI1	13.60	22.30	0.5450
PI2A1	84.80	31.30	0.0087
PI2A2	-45.60	43.30	0.2960
PI2A	60.00	32.60	0.0701
PI2B	-35.10	32.20	0.2800
SRR Variants			
SRR1	27.30	40.50	0.5030
SRR2	-31.00	46.70	0.5090
Sip Protein Variants			
Sip.1a	-19.10	36.60	0.6040
Sip.3a	19.10	36.60	0.6040
Other Virulence factors			
HVGA	-31.00	46.70	0.5090
scpB	-14.30	49.60	0.7750
hylB	44.30	45.00	0.3290
fbsB	-7.25	38.90	0.8530