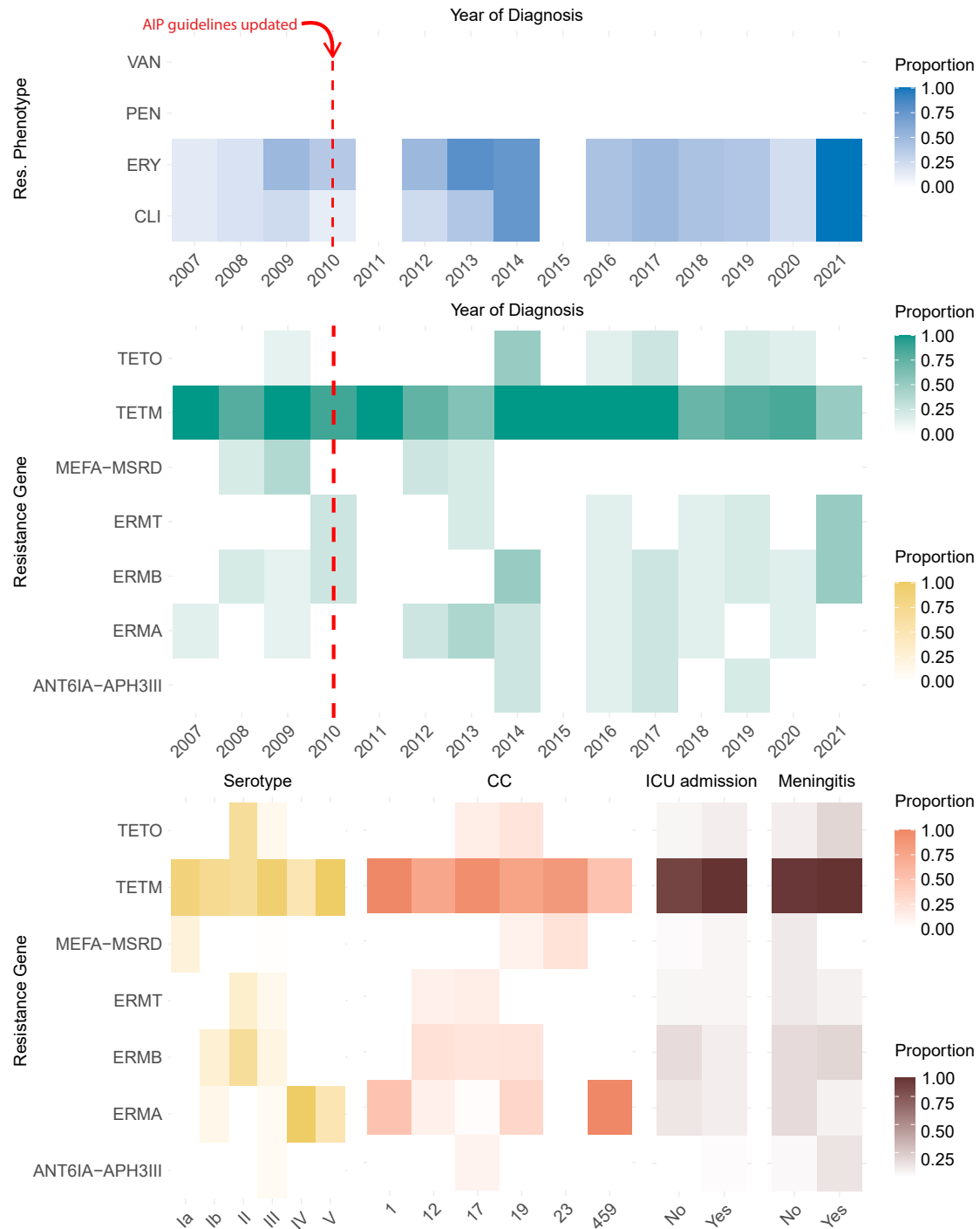


# Supplementary Materials for

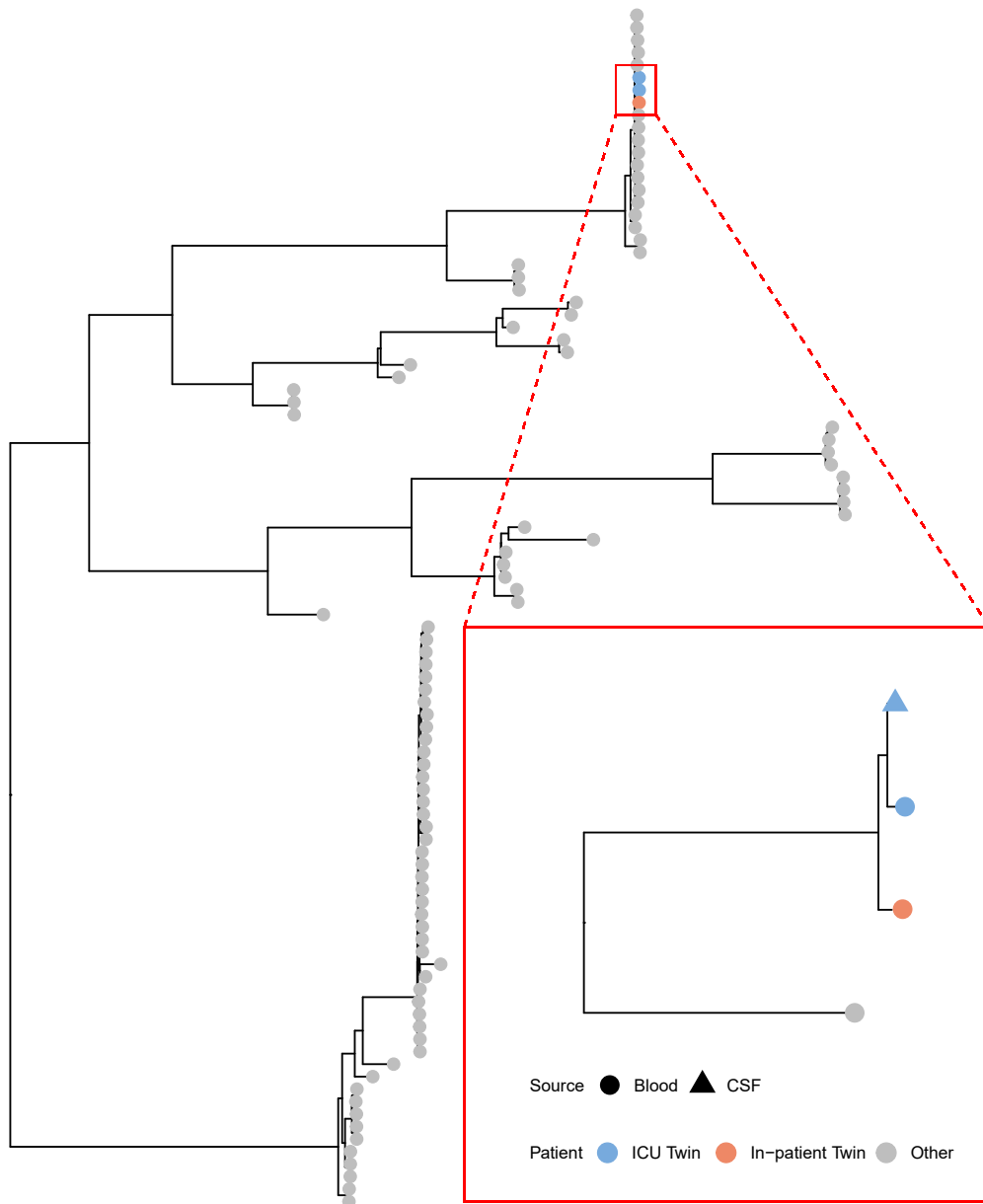
## A 15-year single-centre clinical and genomic analysis of late-onset Group B Streptococcus infection.

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

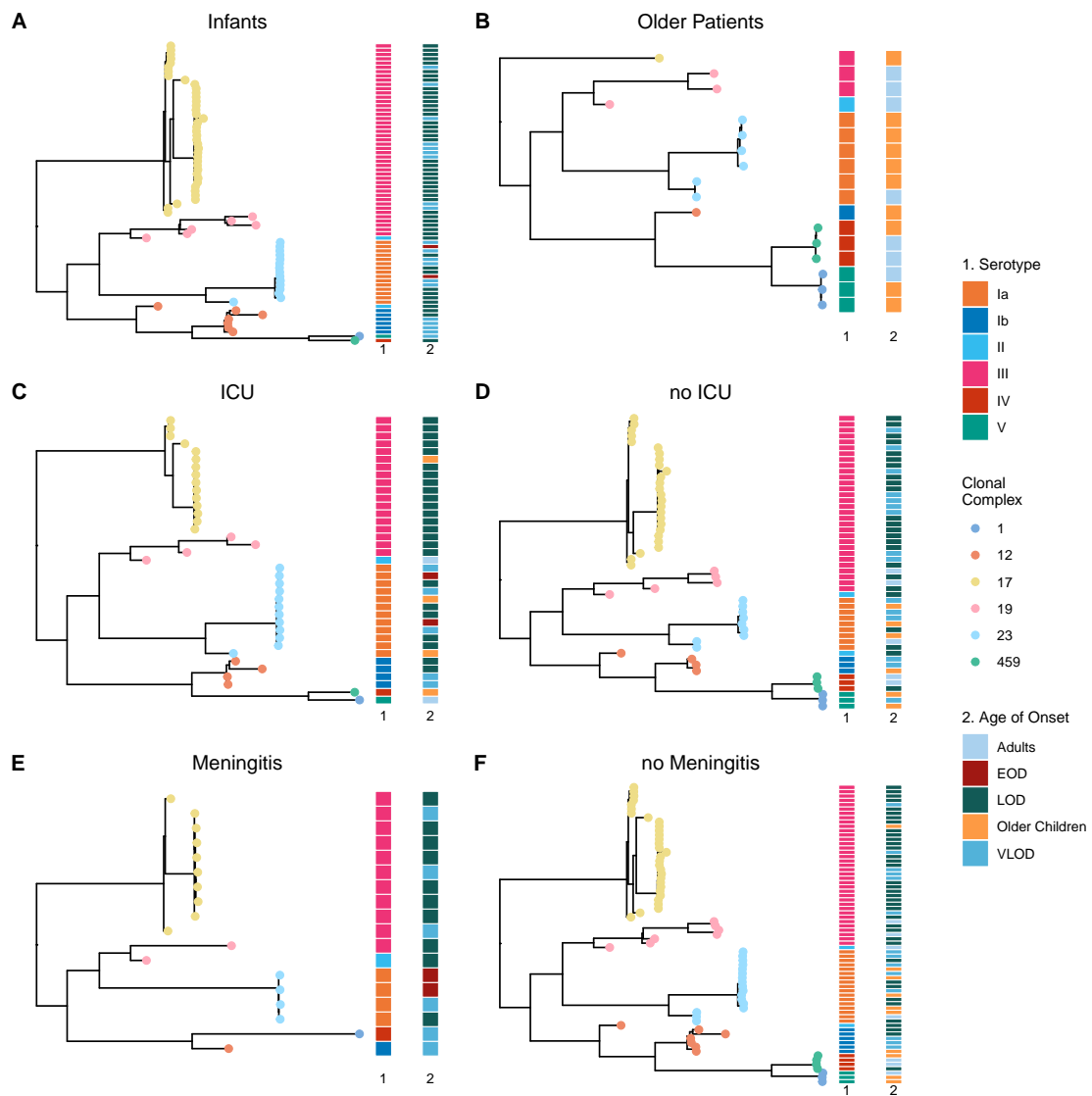
	<b>EOD</b> (N=2)	<b>LOD</b> (N=48)	<b>VLOD</b> (N=20)	<b>Older Children</b> (N=10)	<b>Adults</b> (N=7)	<b>Total Infants</b> (N=70)	<b>Total</b> (N=87)
<b>Serotypes</b>							
Ia	2 (100%)	7 (15%)	6 (30%)	5 (50%)	1 (14%)	15 (21.4%)	21 (24.1%)
Ib	0 (0%)	2 (4%)	4 (20%)	1 (10%)	0 (0%)	6 (8.6%)	7 (8%)
II	0 (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%)
<b>Clonal Complexes (CC)</b>							
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).



**Figure S3. GBS Phylogeny split by age of onset and disease severity.** (A) and (B) are phylogenies containing only infants and older patients with GBS infection, respectively. We observe that CC17-cpsIa is more common among infant cases. (C) and (D) are phylogenies containing only patients admitted to the ICU and those not, respectively.

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

	<b>EOD</b> (N=2)	<b>LOD</b> (N=48)	<b>VLOD</b> (N=20)	<b>Older Children</b> (N=10)	<b>Adults</b> (N=7)	<b>Total</b> (N=87)
<b>CC1</b>						
ST1	0 (0%)	0 (0%)	1 (5%)	2 (20%)	1 (14%)	4
<b>CC12</b>						
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
<b>Total</b>	<b>0 (0%)</b>	<b>3 (6%)</b>	<b>4 (20%)</b>	<b>1 (10%)</b>	<b>0 (0%)</b>	<b>8</b>
<b>CC17</b>						
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
<b>Total</b>	<b>0 (0%)</b>	<b>31 (65%)</b>	<b>9 (45%)</b>	<b>1 (10%)</b>	<b>0 (0%)</b>	<b>41</b>
<b>CC19</b>						
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
<b>Total</b>	<b>0 (0%)</b>	<b>6 (12%)</b>	<b>0 (0%)</b>	<b>0 (0%)</b>	<b>3 (43%)</b>	<b>9</b>
<b>CC23</b>						
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
<b>Total</b>	<b>2 (100%)</b>	<b>7 (15%)</b>	<b>6 (30%)</b>	<b>5 (50%)</b>	<b>1 (14%)</b>	<b>9</b>
<b>CC459</b>						
ST459	0 (0%)	1 (2%)	0 (0%)	1 (10%)	2 (29%)	4
<b>Others</b>						
NF	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1

\* indicates the best scoring allele has  $\geq 1$  mismatch (SNP or indel).

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

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

ST	N (%)	adhP	pheS	atr	glnA	sdhA	glcK	tkr	mismatches
<b>Known STs</b>									
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	
<b>Known STs with mismatches</b>									
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
<b>New ST profile</b>									
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.

	<b>EOD</b> (N=2)	<b>LOD</b> (N=48)	<b>VLOD</b> (N=20)	<b>Older Children</b> (N=10)	<b>Adults</b> (N=7)	<b>Total Infants</b> (N=70)	<b>Total</b> (N=87)
<b>Capsular polysaccharide vaccine</b>							
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%)
<b>Protein subunit vaccine</b>							
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%)
<b>Other Immunogenic Proteins</b>							
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%)
<b>Other Virulence Factors</b>							
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)
<b>Aminoglycosides Resistance</b>							
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%)
<b>Total</b>	<b>0 (0%)</b>	<b>0 (0%)</b>	<b>4 (10%)</b>	<b>0 (0%)</b>	<b>0 (0%)</b>	<b>0 (0%)</b>	<b>4 (5%)</b>
<b>Tetracyclines Resistance</b>							
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%)
<b>Total</b>	<b>4 (100%)</b>	<b>6 (75%)</b>	<b>40 (98%)</b>	<b>8 (89%)</b>	<b>18 (86%)</b>	<b>2 (50%)</b>	<b>78 (90%)</b>
<b>MLSB Resistance</b>							
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%)
<b>Total</b>	<b>2 (50%)</b>	<b>4 (50%)</b>	<b>16 (39%)</b>	<b>5 (56%)</b>	<b>0 (0%)</b>	<b>4 (100%)</b>	<b>31 (36%)</b>
<b>M type Resistance</b>							
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%)
<b>Total</b>	<b>0 (0%)</b>	<b>0 (0%)</b>	<b>0 (0%)</b>	<b>1 (11%)</b>	<b>5 (24%)</b>	<b>0 (0%)</b>	<b>6 (7%)</b>
<b>Fluoroquinolone Resistance</b>							
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%)
<b>Total</b>	<b>0 (0%)</b>	<b>4 (50%)</b>	<b>1 (2%)</b>	<b>0 (0%)</b>	<b>0 (0%)</b>	<b>0 (0%)</b>	<b>5 (6%)</b>

**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
<b>ALP protein family</b>								
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)	<b>0.0030</b>	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)	<b>0.0030</b>	1.12	1.12 (0.72; 1.75)	0.6150
<b>Pilus Islands</b>								
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)	<b>0.0050</b>	1.12	1.12 (0.77; 1.63)	0.5580
<b>SRR Variants</b>								
SRR1	29 (41.4%)	15 (88.2%)	0.09	(0.02 - 0.44)	<b>0.0030</b>	0.97	0.97 (0.63; 1.51)	0.9060
SRR2	40 (57.1%)	1 (5.9%)	21.33	(2.68 - 169.91)	<b>0.0040</b>	1.36	1.36 (0.77; 2.39)	0.2900
<b>Sip Protein Variants</b>								
Sip.1a	8 (11.4%)	9 (52.9%)	0.11	(0.03 - 0.38)	<b>0.0000</b>	0.72	0.72 (0.49; 1.05)	0.0931
Sip.3a	62 (88.6%)	8 (47.1%)	8.72	(2.62 - 29.06)	<b>0.0000</b>	1.39	1.39 (0.95; 2.03)	0.0931
<b>Other Virulence factors</b>								
HVGA	40 (57.1%)	1 (5.9%)	21.33	(2.68 - 169.91)	<b>0.0040</b>	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)	<b>0.0040</b>	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
<b>ALP protein family</b>								
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
<b>Pilus Islands</b>								
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
<b>SRR Variants</b>								
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
<b>Sip Protein Variants</b>								
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
<b>Other Virulence factors</b>								
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=18)	No Meningitis (n=52)	OR	Crude (LR) (95% CI)	P-value	OR	Adjusted (LMM) (95% CI)	P-value
<b>ALP protein family</b>								
ALP1	4 (22.2%)	11 (21.2%)	1.06	(0.29 - 3.89)	0.9240	1.01	(0.79; 1.3)	0.9260
ALP23	1 (5.6%)	1 (1.9%)	3.00	(0.18 - 50.62)	0.4460	1.28	(0.69; 2.39)	0.4330
ALPHA	1 (5.6%)	6 (11.5%)	0.45	(0.05 - 4.03)	0.4760	0.88	(0.62; 1.24)	0.4730
RIB	12 (66.7%)	34 (65.4%)	1.06	(0.34 - 3.29)	0.9210	1.01	(0.81; 1.26)	0.9230
<b>Pilus Islands</b>								
PI1	11 (61.1%)	38 (73.1%)	0.58	(0.19 - 1.79)	0.3420	0.90	(0.72; 1.12)	0.3470
PI2A1	6 (33.3%)	15 (28.8%)	1.23	(0.39 - 3.89)	0.7210	1.04	(0.83; 1.31)	0.7250
PI2A2	2 (11.1%)	4 (7.7%)	1.50	(0.25 - 8.98)	0.6570	1.09	(0.75; 1.57)	0.6610
PI2A	8 (44.4%)	19 (36.5%)	1.39	(0.47 - 4.12)	0.5530	1.07	(0.86; 1.32)	0.5590
PI2B	9 (50%)	29 (55.8%)	0.79	(0.27 - 2.32)	0.6720	0.96	(0.78; 1.18)	0.6770
<b>SRR Variants</b>								
SRR1	7 (38.9%)	22 (42.3%)	0.87	(0.29 - 2.60)	0.8000	0.97	(0.79; 1.2)	0.8030
SRR2	10 (55.6%)	30 (57.7%)	0.92	(0.31 - 2.70)	0.8750	0.98	(0.8; 1.21)	0.8770
<b>Sip Protein Variants</b>								
Sip.1a	3 (16.7%)	5 (9.6%)	1.88	(0.40 - 8.81)	0.4230	1.14	(0.83; 1.58)	0.4250
Sip.3a	15 (83.3%)	47 (90.4%)	0.53	(0.11 - 2.49)	0.4230	0.88	(0.63; 1.21)	0.4250
<b>Other Virulence factors</b>								
HVGA	10 (55.6%)	30 (57.7%)	0.92	(0.31 - 2.70)	0.8750	0.98	(0.8; 1.21)	0.8770
lmb	18 (100%)	51 (98.1%)	2032169.22	(0.00 - Inf)	0.9920	1.30	(0.54; 3.11)	0.5600
scpB	17 (94.4%)	51 (98.1%)	0.33	(0.02 - 5.62)	0.4460	0.78	(0.42; 1.45)	0.4330
hylB	17 (94.4%)	48 (92.3%)	1.42	(0.15 - 13.58)	0.7630	1.06	(0.71; 1.59)	0.7660
fbsB	14 (77.8%)	41 (78.8%)	0.94	(0.26 - 3.43)	0.9240	0.99	(0.77; 1.27)	0.9260

**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
<b>ALP protein family</b>								
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
<b>Pilus Islands</b>								
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
<b>SRR Variants</b>								
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
<b>Sip Protein Variants</b>								
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
<b>Other Virulence factors</b>								
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
<b>ALP protein family</b>								
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
<b>Pilus Islands</b>								
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
<b>SRR Variants</b>								
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
<b>Sip Protein Variants</b>								
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
<b>Other Virulence factors</b>								
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
<b>ALP protein family</b>								
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
<b>Pilus Islands</b>								
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
<b>SRR Variants</b>								
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
<b>Sip Protein Variants</b>								
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
<b>Other Virulence factors</b>								
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 VLOD)

	VLOD (n=20)	LOD (n=48)	OR	Crude (LR) (95% CI)	P-value	OR	Adjusted (LMM) (95% CI)	P-value
<b>Hematological Characteristics</b>								
Hb Mean (SD)	10.9 (1.8)	10.9 (2.4)	1	(0.8-1.3)	0.947			
WBC Mean (SD)	10.6 (6.7)	8.6 (6.2)	1	(0.9-1)	0.243			
Leukocytosis N (%)	8 (40)	15 (32.6)	0.7	(0.2-2.2)	0.563			
Leukopenia N (%)	3 (15)	12 (26.1)	2	(0.5-8.1)	0.563			
Platelet Mean (SD)	290.2 (162.7)	365.2 (152.7)	1	(1-1)	0.083			
ANC Mean (SD)	6.4 (5.8)	5.2 (4.4)	0.9	(0.9-1.1)	0.330			
Neutropenia N (%)	3 (15)	10 (21.7)	1.6	(0.4-6.5)	0.529			
<b>ALP protein family</b>								
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
<b>Pilus Islands</b>								
PII	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
<b>SRR Variants</b>								
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
<b>Sip Protein Variants</b>								
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
<b>Other Virulence factors</b>								
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 ( $\beta$ )	Standard Error	P-value
<b>ALP protein family</b>			
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
<b>Pilus Islands</b>			
PII	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
<b>SRR Variants</b>			
SRR1	27.30	40.50	0.5030
SRR2	-31.00	46.70	0.5090
<b>Sip Protein Variants</b>			
Sip.1a	-19.10	36.60	0.6040
Sip.3a	19.10	36.60	0.6040
<b>Other Virulence factors</b>			
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