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 acros Age Groups

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **EOD** | **LOD** | **VLOD** | **Older**  **Children** | **Adults** | **Total**  **Infants** | **Total** |
| (N=2) | (N=48) | (N=20) | (N=10) | (N=7) | (N=70) | (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%) |

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

# EOD LOD VLOD Older

**Children**

# Adults Total

**CC1**

(N=2) (N=48) (N=20) (N=10) (N=7) (N=87)

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** | **tkt** | **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+ 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%) |

PI2a2+PI2b

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** | |  | |  |  |  |  |  |  |
| PI1 | 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** | **Other** |  | **Crude (LR)** |  |  | **Adjusted (LMM)** | |
| **(n=31)** | | **(n=39)** | **OR** | **(95% CI)** | **P-value** | **OR** | **(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 No Meningitis Crude (LR) Adjusted (LMM)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **(n=18)** | | **(n=52)** | **OR** | **(95% CI)** | **P-value** | **OR** | **(95% CI) P-value** | |
| **ALP protein family** | |  |  |  |  |  |  | |
| 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 | |
| **Pilus Islands** | |  |  |  |  |  |  | |
| 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 |
| **SRR Variants** | |  |  |  |  |  |  |  |
| 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 |
| **Sip Protein Variants** | |  |  |  |  |  |  |  |
| 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 |
| **Other Virulence factors** | |  |  |  |  |  |  |  |
| 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 No Neutropenia Crude (LR) Adjusted (LMM)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **(n=13)** | | **(n=55)** | **OR** | **(95% CI)** | **P-value** | **OR** | **(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 No Leukopenia** | |  | **Crude (LR)** |  |  | **Adjusted (LMM)** | |
| **(n=16)** | | **(n=52)** | **OR** | **(95% CI)** | **P-value** | **OR** | **(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 No Leukocytosis Crude (LR) Adjusted (LMM)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **(n=24)** | | **(n=44)** | **OR** | **(95% CI)** | **P-value** | **OR** | **(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 VLOD)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **VLOD** | **LOD** |  | **Crude (LR)** |  |  | **Adjusted (LMM)** | |
| **(n=20)** | | **(n=48)** | **OR** | **(95% CI)** | **P-value** | **OR** | **(95% CI)** | **P-value** |
| **Hematological Characteristics** | |  |  |  |  |  |  |  |
| 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 |  |  |  |
| **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 Standard P-value probability (***β*) **Error**

**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 facto**  HVGA | **rs**  -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 |