**Supporting information**

**Figure A**

Screened pregnant women > 34 weeks gestation who came for a routine visit to antenatal clinic (n=1562)

Pregnant women eligible for antenatal enrolment (n=1062)

Pregnant women eligible and consent given (n=873)

Cord blood collected (n=541)

Delivered during non-working hours (n=310)

Intrapartum Exclusion (n=22)

Refused Consent (n=189)

**Excluded** (n=500)

Grand multipara mother (n=10), Multiple gestation (n=15), Gestational diabetes (n=63), Hypothyroidism (n=62), Preeclampsia/ Eclampsia (n=63), Fetal congenital anomaly (n=7), Others (n=280)

**Figure A Study profile.** Flowchart showing screening and multi-step selection procedure for collection of information and cord blood.

**Table A. Cell surface markers used for fluorochrome-labeled monoclonal antibody cocktails**

|  |
| --- |
| **Cocktail- A** |
| **Antibody (Clone)** | **Flurochrome** |
| CD45 (2D1) | APC-H7 |
| CD16 (3G8) | PE-Cy7 |
| CD66b (G10F5) | PerCP-Cy5.5 |
| CD14 (M5E2) | FITC |
| CD11c (B-ly6) | V450 |
| CD163 (GHI/61) | APC |
| **Cocktail- B** |
| CD45 (2D1) | APC-H7 |
| CD3 (OKT-3) | PerCP-Cy5.5 |
| CD56 (NACAM16.2) | PE-Cy7 |
| CD4 (RPA-T4) | V450 |
| CD25 (M-A251) | FITC |
| TCR γ/δ (B1) | PE |
| Vα24 Jα18 TCR (6B11) | APC |
| **Cocktail- C** |
| CD45 (2D1) | APC-H7 |
| CD4 (RPA-T4) | V450 |
| CD8 (RPA-T8) | PerCP-Cy5.5 |
| CD45RA (HI100) | PE-Cy7 |
| CD62L (DREG-56) | PE |
| TCR γ/δ (B1) | FITC |
| CD56 (NACAM16.2) | FITC |
| CD25 (M-A251) | FITC |
| **Cocktail- D** |
| CD45 (2D1) | APC-H7 |
| CD19 (HIB19) | APC |
| CD20 (2H7) | PerCP-Cy5.5 |
| CD10 (HI10a) | PE-Cy7 |
| CD43 (10G7) | FITC |
| CD27 (M-T271) | V450 |
| **Cocktail- E** |
| CD45 (2D1) | APC-H7 |
| Lineage 1 (SK7, 3G8, SJ25C1, L27, MφP9, NCAM16.2) | FITC |
| HLA-DR (L243) | PE-Cy7 |
| CD11c (B-ly6) | V450 |
| CD123 (7G3) | APC |

The following fluorochrome-labeled mAbs used on cell-surface markers: CD45, CD16, CD14, CD11c, CD56, CD25, CD3, CD4, CD8, TCRg/d, CD45RA, CD62L, CD19, CD20, CD27, Lineage (LIN: CD3, CD14, CD16, CD19, CD20, CD56), HLA-DR, CD123 were procured from BD Biosciences San Jose, CA; and CD66b, CD163, TCR Vα24 Jα18, CD43, CD10 were procured from BioLegend Inc. San Diego, CA.

**Table B. Comparison of absolute concentrations of immune markers between term SGA and AGA newborns**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Immune markers *a*  | SGA group | AGAgroup | ERC | Adjusted ERC *b* |
|  |  |  | (95% CI) | (95% CI) |
|  |  |  | *P* | *P* |
| Total leukocyte count | n=50 | n=452 |   |   |
| Geometric Mean (95% CI) | 17345 (16119, 18664) | 16781 (16370, 17202) | 1.034 (0.956, 1.118) | 1.024 (0.947, 1.108) |
| Median (IQR) | 17825 (15100, 21050) | 16650 (13725, 20125) | 0.407 | 0.550 |
| Innate immune markers |   |   |   |   |
| Neutrophils  | n=50 | n=450 |   |   |
| Geometric Mean (95% CI) | 10517 (9611, 11509) | 9649 (9357, 9951) | 1.090 (0.989, 1.201) | 1.079 (0.979, 1.189) |
| Median (IQR) | 10770 (8320, 13574) | 9810 (7751, 11946) | 0.081 | 0.126 |
| Myeloid DCs (mDCs)  | n=23 | n=259 |   |   |
| Geometric Mean (95% CI) | 9 (7, 13) | 9 (8, 9) | 1.085 (0.817, 1.440) | 1.074 (0.809, 1.428) |
| Median (IQR) | 7 (6, 17) | 9 (6, 12) | 0.572 | 0.619  |
| Monocytes  | n=50 | n=447 |   |   |
| Geometric Mean (95% CI) | 1352 (1206, 1516) | 1313 (1261, 1366) | 1.030 (0.909, 1.167) | 1.021 (0.901, 1.158) |
| Median (IQR) | 1267 (954, 1756) | 1314 (1031, 1792) | 0.640 | 0.741  |
| Patrolling monocytes | n=48 | n=445 |   |   |
| Geometric Mean (95% CI) | 45 (37, 54) | 45 (43, 48) | 0.998 (0.828, 1.204) | 1.010 (0.836, 1.219) |
| Median (IQR) | 41 (29, 77) | 44 (31, 67) | 0.985 | 0.920  |
| Classical monocytes | n=48 | n=445 |   |   |
| Geometric Mean (95% CI) | 1042 (902, 1204) | 1065 (1022, 1110) | 0.979 (0.856, 1.119) | 0.971 (0.848, 1.111) |
| Median (IQR) | 1100 (752, 1523) | 1103 (803, 1449) | 0.753 | 0.667  |
| Innate like adaptive immune markers |  |  |  |
| NKT cells | n=50 | n=451 |   |   |
| Geometric Mean (95% CI) | 26 (20, 33) | 25 (23, 27) | 1.018 (0.790, 1.312) | 1.022 (0.792, 1.319) |
| Median (IQR) | 28 (13, 54) | 26 (14, 48) | 0.887 | 0.867 |
| Adaptive immune markers |  |  |  |  |
| T lymphocytes  | n=50 | n=451 |   |  |
| Geometric Mean (95% CI) | 2370 (2076, 2705) | 2488 (2384, 2596) | 0.953 (0.832, 1.090) | 0.947 (0.826, 1.085) |
| Median (IQR) | 2370 (1694, 3510) | 2598 (1863, 3394) | 0.480 | 0.429 |
| CD4+ T cells | n=50 | n=450 |   |  |
| Geometric Mean (95% CI) | 1575 (1379, 1799) | 1685 (1614, 1759) | 0.935 (0.816, 1.071) | 0.925 (0.807, 1.061) |
| Median (IQR)  | 1535 (1159, 2390) | 1784 (1277, 2317) | 0.331 | 0.265  |
| Naive CD4+ T cells  | n=50 | n=448 |   |  |
| Geometric Mean (95% CI) | 1528 (1343, 1739) | 1628 (1559, 1700) | 0.939 (0.819, 1.076) | 0.931 (0.812, 1.069) |
| Median (IQR)  | 1525 (1107, 2096) | 1732 (1229, 2224) | 0.364 | 0.311 |
| T regulatory cells | n=50 | n=449 |   |  |
| Geometric Mean (95% CI) | 186 (163, 213) | 191 (183, 199) | 0.976 (0.850, 1.120) | 0.969 (0.843, 1.113) |
| Median (IQR)  | 186 (139, 277) | 193 (145, 259) | 0.728 | 0.655  |
| CD8+ T cells  | n=50 | n=447 |   |  |
| Geometric Mean (95% CI) | 852 (751, 966) | 835 (798, 873) | 1.020 (0.886, 1.174) | 1.023 (0.888, 1.179) |
| Median (IQR)  | 842 (611, 1259) | 844 (610, 1176) | 0.783 | 0.750  |
| Naïve CD8+ T cells | n=50 | n=447 |   |   |
| Geometric Mean (95% CI) | 783.6 (691.6, 887.9) | 764.3 (730.3, 799.8) | 1.025 (0.890, 1.182) | 1.029 (0.892, 1.187) |
| Median (IQR) | 782.3 (572, 1107.6) | 769.2 (560.9, 1089.1) | 0.729 | 0.692 |
| Immunoglobulin |  |  |  |  |
| IgA, mg/dL *c* | n=53 | n=459 |   |  |
| Geometric Mean (95% CI) | 0.74 (0.59, 0.94) | 0.71 (0.66, 0.75) | 1.047 (0.856, 1.280) | 1.037 (0.847, 1.270) |
| Median (IQR) | 0.81 (0.42, 1.16) | 0.69 (0.44, 1.11) | 0.654 | 0.725 |

*a* All immune marker variables have been log transformed

*b*Adjusted for pre-specified factors: maternal age & newborn gender

*c* To convert IgA in mg/dL to SI unit (mg/L) multiply by 10

SGA, small for gestational age (birth weight below the 10th centile or 2SD below mean for GA of reference/normal birth curves); AGA, appropriate for gestational age (birth weight between the 10th and 90th centile for GA of reference/normal birth curves); ERC, exponentiated regression coefficient, ordinary least square (OLS) regression analysis after log transformation of dependent variable (immune marker); 95% CI, 95 percent confidence interval.

**Table C. Comparison of relative frequencies of immune markers between term SGA and AGA newborns**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Immune markers *a* | SGA Group | AGAGroup | ERC | Adjusted ERC *b* |
|  |  |  | (95% CI) | (95% CI) |
|  |  |  | *P* | *P* |
| Innate immune markers |  |  |  |  |
| CD56bright NK cells | n=50 | n=450 |   |   |
| Geometric Mean (95% CI) | 7.87 (6.73, 9.21) | 8.09 (7.73, 8.47) | 0.973 (0.840, 1.128) | 0.981(0.846, 1.138) |
| Median (IQR) | 8.83 (5.17, 11.0) | 8.00 (6.10, 11.0) |  0.718 | 0.803  |
| Monocytes  | n=50 | n=447 |   |   |
| Geometric Mean (95% CI) | 7.80 (7.04, 8.64) | 7.82 (7.59, 8.05) | 0.997 (0.908, 1.096) | 0.998 (0.908, 1.097) |
| Median (IQR) | 7.93 (6.1, 10.0) | 8.0 (6.52, 9.54) | 0.956 | 0.966  |
| Patrolling monocytes | n=48 | n=445 |   |   |
| Geometric Mean (95% CI) | 3.71 (3.18, 4.33) | 3.71 (3.52, 3.90) | 1.000 (0.849, 1.179) | 1.019 (0.865, 1.200) |
| Median (IQR) | 3.61 (2.44, 4.81) | 3.76 (2.76, 5.08)  | 0.996 | 0.826  |
| Innate like adaptive immune markers |  |  |  |
| NKT cells | n=50 | n=451 |   |   |
| Geometric Mean (95% CI) | 1.08 (0.82, 1.44) | 1.01 (0.93, 1.10) | 1.069 (0.818, 1.398) | 1.080 (0.824, 1.414) |
| Median (IQR) | 1.15(0.47, 2.07) | 1.05 (0.56, 1.86) | 0.624 | 0.577  |
| iNKT cells | n=17 | n=170 |   |  |
| Geometric Mean (95% CI) | 0.29 (0.20, 0.41) | 0.28 (0.25, 0.32) | 1.008 (0.685, 1.481) | 1.009 (0.683, 1.489) |
| Median (IQR) | 0.22 (0.16, 0.47 | 0.26 (0.17, 0.43) | 0.969 | 0.965 |
| TCR γδ cells  | n=49 | n=448 |   |  |
| Geometric Mean (95% CI) | 3.89 (3.37, 4.50) | 4.14 (3.96, 4.34) | 0.939 (0.812, 1.087) | 0.944 (0.815, 1.093) |
| Median (IQR) | 3.66 (2.75, 5.34) | 4.24 (3.08, 5.52) |  0.398 | 0.440 |
| B1B cells | n=50 | n=449 |   |  |
| Geometric Mean (95% CI)Median (IQR) | 1.02 (0.85, 1.23)1.06 (0.8, 1.57) | 1.02 (0.97, 1.08)1.08 (0.77, 1.5) | 0.997 (0.832, 1.195)0.973 | 0.988 (0.823, 1.186)0.900 |
| Adaptive immune markers |  |  |  |  |
| T lymphocytes  | n=50 | n=451 |   |  |
| Geometric Mean (95% CI) | 13.6 (12.2, 15.3) | 14.8 (14.2, 15.4) | 0.921 (0.814, 1.042) | 0.923 (0.815, 1.045) |
| Median (IQR) | 13.7 (11.0, 18.5) | 15.4 (11.5, 20.0) | 0.192 | 0.205 |
| Naive CD4+ T cells  | n=50 | n=448 |  |  |
| Geometric Mean (95% CI) | 96.1 (95.6, 96.6)  | 96.5 (96.4, 96.7)  | 0.995 (0.991, 1.001) | 0.995 (0.990, 1.001) |
| Median (IQR)  | 96.0 (95.0, 97.5) | 97.0 (96.0, 98.0) | 0.092 | 0.095  |
| T regulatory cells | n=50 | n=449 |   |  |
| Geometric Mean (95% CI) | 1.06 (0.94, 1.21) | 1.14 (1.09, 1.19) | 0.934 (0.818, 1.066) | 0.933 (0.816, 1.066) |
| Median (IQR)  | 1.05 (0.79, 1.50) | 1.14 (0.89, 1.55) | 0.308 | 0.307  |
| CD8+ T cells  | n=50 | n=447 |   |  |
| Geometric Mean (95% CI) | 4.91 (4.36, 5.53) | 4.98 (4.78, 5.19)  | 0.986 (0.867, 1.121) | 0.998 (0.877, 1.135) |
| Median (IQR)  | 5.32 (3.53, 6.50) | 5.0 (3.78, 6.70) | 0.826 | 0.973 |
| Naïve CD8+ T cells | n=50 | n=447 |   |   |
| Geometric Mean (95% CI) | 92 (90.7, 93.4) | 91.1 (90.8, 93.4) | 1.005 (0.989, 1.022) | 1.006 (0.989, 1.023) |
| Median (IQR) | 93.3 (90.1, 95.3) | 93 (89.3, 95.1) | 0.537 | 0.498 |
| Naïve B cells | n=50 | n=449 |   |  |
| Geometric Mean (95% CI) | 96.4 (95.7, 97.1) | 96.6 (96.4, 96.8) | 0.998 (0.991, 1.005) | 0.997(0.991, 1.004) |
| Median (IQR) | 96.9 (96.0, 98.0) | 97.0 (95.7, 98.0) | 0.571 | 0.474 |
| CD10+ Naïve B cells | n=50 | n=440 |   |  |
| Geometric Mean (95% CI) | 22.2 (20.0, 24.7) | 23.6 (22.8, 24.4) | 0.943 (0.849, 1.046) | 0.929 (0.837, 1.032) |
| Median (IQR) | 22.6 (18.1, 28.8) | 23.5 (19.1, 30.5) | 0.266 | 0.169 |

*a*All immune marker variables have been log transformed

*b*Adjusted for pre-specified factors: maternal age & newborn gender

SGA, small for gestational age (birth weight below the 10th centile or 2SD below mean for GA of reference/normal birth curves); AGA, appropriate for gestational age (birth weight between the 10th and 90th centile for GA of reference/normal birth curves); ERC, exponentiated regression coefficient, ordinary least square (OLS) regression analysis after log transformation of dependent variable (immune marker); 95% CI, 95 percent confidence interval.

**Table D. Characteristics of participant population in the four hospital sites**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Characteristics *a*  |  |  Total |  MAMC | SJH | AIIMS | GHG |
|  |  | n=502 | n=276 | n=178 | n=21 | n=27 |
| Parental  |  |  |  |  |  |  |
| Mother’s age, (years) |  | 24.3 (3.4) | 24.9 (3.5) | 23.6 (3.2) | 24.4 (3.6) | 23.4 (2.8) |
| Father’s age, (years)  |  | 28.2 (3.7) | 28.4 (3.8) | 27.9 (3.5) | 29.0 (3.2) | 27.7 (4.4) |
|   |  | n=411  | n=256  | n=133 | n=19 | n=3 |
| Mother’s intrapartum weight, kg  |  |  58.0 (9.0) |  58.3 (8.8) | 55.9 (8.3) | 66.6 (8.3) | 59.7 (18.5) |
|   |  |  n=454 |  n=272 | n=147 | n=20 | n=15 |
| Mother’s height, cm  |  |  152.2 (4.8) |  152.5 (3.6) | 151.4 (6.1) | 155.9 (5.4) | 151.2 (6.5) |
| Mother’s education status, (in years)  |  |  9.0 (4.0) |  9.0 (4.0) | 9.0 (5.0) | 12.0 (4.0) | 9.0 (5.0) |
| Father’s education status (in years)  |  | 10.0 (4.0)  | 10.0 (4.0)  | 11.0 (4.0) | 13.0 (4.0) | 11.0 (3.0) |
| Neonatal  |  |  |  |  |  |  |
| Female  | n (%) | 247 (49.2) | 150 (54.3) | 74 (41.8) | 7 (33.3) | 16 (59.3) |
| Gestational age at birth, (weeks)  |  |  39 (1.1) |  39 (1.0) | 39 (1.1) | 38 (1.1) | 39 (1.1) |
| Birth weight, kg |  |  2.9 (0.4) |  2.85 (0.38) | 2.95 (0.41) | 2.84 (0.40) | 3.07 (0.40) |
|   |  |  n=497 |  n=276 | n=178 | n=16 | n=27 |
| Length, cm  |  |  49.97 (1.8) |  50.0 (0.9) | 49.8 (1.9) | 47.5 (3.6) | 51.8 (3.9) |
|   |  |  n=497 |  n=276 | n=178 | n=16 | n=27 |
| Head circumference, cm  |  |  34.2 (1.2) |  34.4 (0.9) | 34.0 (1.3) | 35.2 (3.3) | 34.0 (1.3) |
|   |  |  n=494 |  n=272 | n=178 | n=19 | n=25 |
| Cord blood serum zinc level, µg/dL***b***  |  | 79.2 (18.3)  | 80.9 (17.5)  | 80.2 (18.5) | 71.2 (19.6) | 60.7 (11.3) |

*a* All values are Mean (SD) except where specified

*b* To convert zinc in µg/dL to SI unit (µmol/L) multiply by 0.153

 SGA, small for gestational age (birth weight below the 10th centile or 2SD below mean for GA of reference/normal birth curves); AGA, appropriate for gestational age (birth weight between the 10th and 90th centile for GA of reference/normal birth curves)

**Table E. Comparison of absolute concentrations of immune markers in term AGA newborns between the hospital sites**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Immune markers*a* | Total AGA group | MAMC  | SJH | AIIMS | GHG |
|  |  | AGA group | AGA group | AGA group | AGA group |
| Total leukocyte count | n=452 | n=247 | n=158 | n=20 | n=27 |
| Geometric Mean (95% CI) | 16781 (16370, 17202) | 16740 (16206, 17292) | 17069 (16370, 17797) | 13367 (12152, 14704) | 18386 (16832, 20907) |
| Median (IQR) | 16650 (13725, 20125) | 16650 (13750, 20150) | 17200 (13900, 19900) | 13725 (11425, 15125) | 18950 (14700, 24100) |
| Innate immune markers |   |   |   |   |   |
| Neutrophils  | n=450 | n=246 | n=157 | n=20 | n=27 |
| Geometric Mean (95% CI) | 9649 (9357, 9951) | 9912 (9535, 10302) | 9444 (8946, 9970) | 7055 (6102, 8156) | 10801 (9363, 12461) |
| Median (IQR) | 9810 (7751, 11946) | 10052 (7982, 12128) | 9730 (7700, 11946) | 7606 (5663, 8901) | 11112 (8195, 13292) |
| Dendritic cells (DCs) | n=419 | n=229 | n=144 | n=19 | n=27 |
| Geometric Mean (95% CI) | 56 (53, 59) | 52 (49, 57) | 60 (55, 66) | 57 (45, 71) | 60 (46, 79) |
| Median (IQR) | 56 (53, 82) | 54 (37, 79) | 60 (38, 86) | 60 (41, 83) | 51 (39, 92) |
| Myeloid DCs (mDCs)  | n=259 | n=138 | n=93 | n=1 | n=27 |
| Geometric Mean (95% CI) | 9 (8, 9) | 8 (7, 9) | 10 (8, 11) | 11 (-, -) | 9 (7, 12) |
| Median (IQR) | 9 (6, 12) | 8 (5, 11) | 10 (7, 14) | 11 (11, 11) | 11 (6, 13) |
| Plasmacytoid DCs (pDCs) | n=259 | n=138 | n=93 | n=1 | n=27 |
| Geometric Mean (95% CI) | 9 (8, 10) | 9 (8, 10) | 9 (7, 11) | 6 (-, -) | 10 (8, 13) |
| Median (IQR) | 10 (6, 14) | 10 (6, 14) | 11 (5, 16) | 6 (6, 6) | 9 (7, 14) |
| mDC:pDC ratio | n=259 | n=138 | n=93 | n=1 | n=27 |
| Geometric Mean (95% CI) | 0.95 (0.88, 1.03) | 0.87 (0.79, 0.97) | 1.07 (0.93, 1.23) | 1.8 (-, -) | 0.94 (0.73, 1.38) |
| Median (IQR) | 0.96 (0.61, 1.42) | 0.90 (0.60, 1.37) | 1.02 (0.69, 1.60) | 1.8 (1.8, 1.8) | 0.96 (0.61, 1.48) |
| Natural Killer (NK) cells | n=451 | n=247 | n=157 | n=20 | n=27 |
| Geometric Mean (95% CI) | 768 (730, 807) | 722 (677, 771) | 855 (781, 935) | 866 (695, 1079) | 658 (519, 833) |
| Median (IQR) | 785 (522, 1124) | 709 (505, 1047) | 907 (586, 1226) | 791 (650, 1267) | 607 (412, 1150) |
| CD56bright NK cells | n=450 | n=246 | n=158 | n=19 | n=27 |
| Geometric Mean (95% CI) | 62 (59, 66) | 60 (55, 64) | 67 (61, 75) | 84 (61, 117) | 48 (38, 59) |
| Median (IQR) | 63 (42, 94) | 59 (42, 91) | 66 (44, 108) | 75 (66, 119) | 44 (34, 78) |
| Monocytes  | n=447 | n=245 | n=155 | n=20 | n=27 |
| Geometric Mean (95% CI) | 1313 (1261, 1366) | 1277 (1212, 1345) | 1430 (1341, 1524) | 925 (694, 1233) | 1337 (1139, 1569) |
| Median (IQR) | 1314 (1031, 1792) | 1306 (1031, 1697) | 1466 (1063, 1921) | 966 (841, 1344) | 1413 (1058, 1662) |
| Patrolling monocytes | n=445 | n=244 | n=156 | n=18 | n=27 |
| Geometric Mean (95% CI) | 45 (43, 48) | 42 (39, 46) | 51 (46, 56) | 44 (32, 61) | 43 (35, 53) |
| Median (IQR) | 44 (31, 67) | 42 (27, 61) | 49 (34, 74) | 48 (20, 71) | 50 (33, 67) |
| Classical monocytes | n=445 | n=244 | n=156 | n=18 | n=27 |
| Geometric Mean (95% CI) | 1065 (1022, 1110) | 1032 (975, 1092) | 1142 (1067, 1222) | 881 (709, 1095) | 1080 (895, 1303) |
| Median (IQR) | 1103 (803, 1449) | 1090 (774, 1394) | 1161 (868, 1567) | 879 (775, 1201) | 1043 (880, 1435) |
| Inflammatory monocytes | n=445 | n=244 | n=156 | n=18 | n=27 |
| Geometric Mean (95% CI) |  55 (51, 58) |  52 (48, 56) |  61 (55, 68) |  42 (30, 60) |  56 (43, 74) |
| Median (IQR) | 55 (36, 84) | 52 (35, 84) | 58 (39, 95) | 39 (29, 74) | 60 (34, 81) |
| Innate like adaptive immune markers |  |  |  |  |
| NKT cells | n=451 | n=247 | n=157 | n=20 | n=27 |
| Geometric Mean (95% CI) | 25 (23, 27) | 24 (21, 26) | 28 (24, 31) | 50 (38, 68) | 17 (14, 22) |
| Median (IQR) | 26 (14, 48) | 26 (15, 44) | 28 (14, 55) | 48 (31, 65) | 16 (10, 26) |
| iNKT cells | n=170 | n=76 | n=62 | n=5 | n=27 |
| Geometric Mean (95% CI) | 4.1 (3.6, 4.7) | 3.9 (3.2, 4.8) | 4.1 (3.2, 5.2) | 1.9 (1.0, 3.6) | 5 (4, 7) |
| Median (IQR) | 4.7 (2.5, 7.8) | 4.3 (2.2, 8.1) | 4.9 (2.4, 7.9) | 1.7 (1.6, 1.8) | 5 (4, 8) |
| TCR γδ cells  | n=448 | n=245 | n=156 | n=20 | n=27 |
| Geometric Mean (95% CI) | 103 (97, 109) | 97 (90, 104) | 111 (100, 123) | 78 (60, 102) | 152 (123, 188) |
| Median (IQR) | 106 (69, 162) | 100 (66, 147) | 114 (76, 168) | 84 (49 107) | 143 (113, 212) |
| B1B cells | n=449 | n=246 | n=157 | n=19 | n=27 |
| Geometric Mean (95% CI) | 5 (5, 5) | 5 (4, 5) | 5 (5, 6) | 4 (3, 6) | 6 (4, 10) |
| Median (IQR) | 5 (3, 9) | 5 (3, 9) | 6 (3, 9) | 5 (3, 6) | 8 (3, 13) |
| Adaptive immune markers |  |  |  |  |  |
| T lymphocytes  | n=451 | n=247 | n=157 | n=20 | n=27 |
| Geometric Mean (95% CI) | 2488 (2384, 2596) | 2357 (2227, 2456) | 2674 (2479, 2884) | 2415 (2142, 2722) | 2737 (2278, 3290) |
| Median (IQR) | 2598 (1863, 3394) | 2347 (1689, 2347) | 2763 (2063, 3510) | 2424 (2029, 2915) | 3046 (1882, 3880) |
| CD4+ T cells | n=450 | n=247 | n=156 | n=20 | n=27 |
| Geometric Mean (95% CI) | 1685 (1614, 1759) | 1691 (1406, 2033) | 1805 (1673, 1946) | 1746 (1541, 1978) | 1754 (1462, 2104) |
| Median (IQR)  | 1784 (1277, 2317) | 1709 (1168, 2250) | 1888 (1407, 2472) | 1770 (1426, 2213) | 1944 (1283, 2445) |
| Naive CD4+ T cells  | n=448 | n=246 | n=155 | n=20 | n=27 |
| Geometric Mean (95% CI) | 1628 (1559, 1700) | 1546 (1456, 1641) | 1754 (1629, 1888) | 1682 (1486, 1904) | 1663 (1363, 2030) |
| Median (IQR)  | 1732 (1229, 2224) | 1620 (1145, 2163) | 1852 (1359, 2421) | 1673 (1372, 2124) | 1759 (1252, 2224) |
| T regulatory cells | n=449 | n=247 | n=155 | n=20 | n=27 |
| Geometric Mean (95% CI) | 191 (183, 199) | 186 (175, 198) | 199 (186, 213) | 197 (159, 245) | 185 (151, 225) |
| Median (IQR)  | 193 (145, 259) | 188 (141, 257) | 204 (149, 265) | 195 (140, 228) | 204 (135, 250) |
| CD8+ T cells  | n=447 | n=245 | n=155 | n=20 | n=27 |
| Geometric Mean (95% CI) | 835 (798, 873) | 795 (748, 844) | 896 (831, 967) | 753 (626, 906) | 941 (751, 1180) |
| Median (IQR)  | 844 (610, 1176) | 800 (592, 1149) | 870 (658, 1245) | 791 (568, 935) | 948 (644, 1497) |
| Naïve CD8+ T cells | n=447 | n=245 | n=155 | n=20 | n=27 |
| Geometric Mean (95% CI) | 764.3 (730.3, 799.8) | 729 (686, 775) | 820 (760, 884) | 676 (560, 816) | 859 (681, 1083) |
| Median (IQR) | 769.2 (560.9, 1089.1) | 729 (548, 1077) | 809 (623, 1128) | 724 (520, 858) | 890 (615, 1301) |
| CD4:CD8 T cell ratio | n=447 | n=245 | n=155 | n=20 | n=27 |
| Geometric Mean (95% CI) | 2.02 (1.96, 2.09) | 2.0 (1.9, 2.1) | 2.0 (1.9, 2.2) | 2.3 (2.0, 2.7) | 1.9 (1.6, 2.5) |
| Median (IQR) | 2.02 (1.60, 2.53) | 2.0 (1.6, 2.5) | 2.0 (1.5, 2.6) | 2.3 (1.9, 2.7) | 1.7 (1.5, 2.3) |
| Naïve CD4:CD8 T cell ratio | n=447 | n=245 | n=155 | n=20 | n=27 |
| Geometric Mean (95% CI) | 2.13 (2.05, 2.21) | 2.0 (1.9, 2.1) | 2.0 (1.9, 2.1) | 2.3 (2.0, 2.6) | 1.9 (1.6, 2.2) |
| Median (IQR) | 2.14 (1.65, 2.78) | 1.9 (1.5, 2.5) | 2.0 (1.5, 2.5) | 2.2 (1.9, 2.7) | 1.8 (1.5, 2.2) |
| Naïve B cells | n=449 | n=246 | n=157 | n=19 | n=449 |
| Geometric Mean (95% CI) | 473 (444, 503) | 450 (415, 487) | 511 (458, 571) | 427 (297, 613) | 547 (428, 698) |
| Median (IQR) | 475 (314, 730) | 452 (309, 661) | 587 (330, 793) | 465 (287, 745) | 524 (319, 889) |
| CD10+ Naïve B cells | n=440 | n=240 | n=155 | n=19 | n=440 |
| Geometric Mean (95% CI) | 116 (108, 124) | 109 (99, 119) | 124 (109, 141) | 119 (83, 171) | 122 (95, 157) |
| Median (IQR) | 123 (73, 186) | 115 (73, 174) | 133 (73, 210) | 132 (69, 220) | 102 (83, 181) |
| Immunoglobulin |  |  |  |  |  |
| IgM, mg/dL*b* | n=468 | n=256 | n=166 | n=17 | n=29 |
| Geometric Mean (95% CI) | 7.05 (6.69, 7.44) | 7.3 (6.8, 7.8) | 6.7 (6.1, 7.3) | 6.7 (4.7, 9.6) | 7 (6, 9) |
| Median (IQR) | 7.15 (4.52, 10.56) | 7.3 (4.5, 10.9) | 6.7 (4.5, 9.7) | 4.9 (4.5, 9.7) | 8 (5, 12) |
| IgA, mg/dL *b* | n=459 | n=251 | n=160 | n=19 | n=29 |
| Geometric Mean (95% CI) | 0.71 (0.66, 0.75) | 0.55 (0.51, 0.59) | 1.03 (0.93, 1.14) | 0.80 (0.55, 1.17) | 0.78 (0.65, 0.95) |
| Median (IQR) | 0.69 (0.44, 1.11) | 0.56 (0.36, 0.84) | 1.04 (0.67, 1.46) | 0.69 (0.42, 1.48) | 0.72 (0.56, 1.08) |

*a* All immune marker (IM) variables have been log transformed

*b,* To convert IgM and IgA in mg/dL to SI unit (mg/L) multiply by 10

SGA, small for gestational age (birth weight below the 10th centile or 2SD below mean for GA of reference/normal birth curves); AGA, appropriate for gestational age (birth weight between the 10th and 90th centile for GA of reference/normal birth curves); ERC,exponentiated regression coefficient, ordinary least square (OLS) regression analysis after log transformation of dependent variable (immune marker); 95% CI, 95 percent confidence interval.

**Table F. Comparison of relative frequencies of immune markers in term AGA newborns between the hospital sites**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Immune markers *a*  | AGAgroup | MAMC | SJH | AIIMS | GHG |
|  |  | AGA group | AGAgroup | AGAgroup | AGAgroup |
| Innate immune markers |  |  |  |  |  |
| Neutrophils  | n=450 | n=246 | n=157 | n=20 | n=27 |
| Geometric Mean (95% CI) | 57.5 (56.6, 58.4) | 59 (58, 60) | 55.3 (53.7, 56.9) | 57.5 (56.6, 58.4) | 58.7 (55.8, 61.9) |
| Median (IQR) | 58.4 (52.6, 64.7) | 60 (55, 66) | 56.3 (50.2, 63.1) | 54.5 (47.6, 57.7) | 58.4 (53.3, 65.9) |
| Dendritic cells (DCs) | n=419 | n=229 | n=144 | n=19 | n=27 |
| Geometric Mean (95% CI) | 0.33 (0.32, 0.35) | 0.32 (0.30, 0.34) | 0.35 (0.32, 0.37) | 0.4 (0.3, 0.5) | 0.33 (0.26, 0.41) |
| Median (IQR) | 0.34 (0.24, 0.46) | 0.32 (0.23, 0.45) | 0.35 (0.27, 0.46) | 0.4 (0.3, 0.7) | 0.32 (0.23, 0.43) |
| Myeloid DCs (mDCs)  | n=259 | n=138 | n=93 | n=1 | n=27 |
| Geometric Mean (95% CI) | 14.2 (13.2, 15.2) | 14 (13, 15) | 14.3 (12.7, 16.2) | 12.8 (-, -) | 16 (12, 20) |
| Median (IQR) | 14.5 (9.7, 22.0) | 14 (9, 22) | 15.0 (10.0, 22.0) | 12.8 (12.8, 12.8) | 17 (10, 24) |
| Plasmacytoid DCs (pDCs) | n=259 | n=138 | n=93 | n=1 | n=27 |
| Geometric Mean (95% CI) | 14.9 (13.8, 16.2) | 16 (14, 17) | 13.4 (11.4, 15.7) | 7.3 (-, -) | 17 (13, 21) |
| Median (IQR) | 15.8 (10.2, 24.4) | 15 (11, 25) | 15.6 (8.8, 23.8) | 7.3 (7.3, 7.3) | 18 (10, 28) |
| Natural Killer (NK cells) | n=451 | n=247 | n=157 | n=20 | n=27 |
| Geometric Mean (95% CI) | 4.57 (4.36, 4.79) | 4.3 (4.1, 4.6) | 5.0 (4.6, 5.4) | 6.4 (5.2, 7.9) | 3.6 (2.9, 4.4) |
| Median (IQR) | 4.66 (3.36, 6.47) | 4.3 (3.1, 6.2) | 5.4 (3.7, 7.4) | 6.5 (4.3, 8.5) | 3.4 (2.4, 5.3) |
| CD56bright NK cells | n=450 | n=246 | n=158 | n=19 | n=27 |
| Geometric Mean (95% CI) | 8.09 (7.73, 8.47) | 8.2 (7.8, 8.7) | 7.9 (7.3, 8.6) | 8.9 (6.8, 11.7) | 7.2 (6.1, 8.6) |
| Median (IQR) | 8.00 (6.10, 11.0) | 8.2 (6.4, 10.8) | 7.6 (5.8, 11.5) | 9.2 (6.8, 11.3) | 7.3 (5.7, 10.0) |
| Monocytes  | n=447 | n=245 | n=155 | n=20 | n=27 |
| Geometric Mean (95% CI) | 7.82 (7.59, 8.05) | 7.6 (7.3, 7.9) | 8.4 (8.0, 8.8) | 6.9 (5.3, 9.1) | 7.3 (6.7, 7.9) |
| Median (IQR) | 8.0 (6.52, 9.54) | 7.8 (6.4, 9.1) | 8.7 (6.8, 10.2) | 8.1 (6.4, 9.7) | 7.1 (6.2, 8.6) |
| Patrolling monocytes | n=445 | n=244 | n=156 | n=18 | n=27 |
| Geometric Mean (95% CI) | 3.71 (3.52, 3.90) | 3.6 (3.3, 3.9) | 3.9 (3.6, 4.2) | 4.3 (3.4, 5.4) | 3.5 (2.8, 4.4) |
| Median (IQR) | 3.76 (2.76, 5.08)  | 3.6 (2.6, 5.0)  | 4.0 (2.9, 5.3)  | 4.4 (3.5, 5.0)  | 4.2 (2.4, 5.2)  |
| Classical monocytes | n=445 | n=244 | n=156 | n=18 | n=27 |
| Geometric Mean (95% CI) | 87.6 (87.0, 88.1) | 88 (87, 89) | 87.3 (86.4, 88.2) | 86.0 (83.2, 88.9) | 88 (86, 90) |
| Median (IQR) | 88.7 (85.1, 91.5) | 89 (85, 92) | 88.2 (85.0, 91.1) | 88.2 (82.9, 90.2) | 88 (86, 91) |
| Inflammatory monocytes | n=445 | n=244 | n=156 | n=18 | n=27 |
| Geometric Mean (95% CI) | 4.49 (4.26, 4.74) | 4.4 (4.1, 4.7) | 4.7 (3.6, 6.2) | 4.1 (3.1, 5.5) | 4.6 (3.8, 5.5) |
| Median (IQR) | 4.6 (3.07, 6.66) | 4.4 (3.0, 6.7) | 4.7 (3.1, 7.3) | 4.3 (3.0, 5.6) | 4.4 (3.4, 6.3) |
| Innate like adaptive immune markers |  |  |  |  |
| NKT cells | n=451 | n=247 | n=157 | n=20 | n=27 |
| Geometric Mean (95% CI) | 1.01 (0.93, 1.10) | 1.0 (0.9, 1.1) | 1.0 (0.9, 1.2) | 2.1 (1.5, 2.8) | 0.6 (0.5, 0.8) |
| Median (IQR) | 1.05 (0.56, 1.86) | 1.1 (0.6, 1.8) | 1.0 (0.6, 1.9) | 2.0 (1.3, 2.8) | 0.6 (0.5, 0.9) |
| iNKT cells | n=170 | n=76 | n=62 | n=5 | n=27 |
| Geometric Mean (95% CI) | 0.28 (0.25, 0.32) | 0.36 (0.29, 0.44) | 0.24 (0.20, 0.28) | 0.36 (0.16, 0.82) | 0.21 (0.18, 0.26) |
| Median (IQR) | 0.26 (0.17, 0.43) | 0.33 (0.21, 0.58) | 0.23 (0.15, 0.32) | 0.28 (0.28, 0.53) | 0.22 (0.17, 0.28) |
| TCR γδ cells  | n=448 | n=245 | n=156 | n=20 | n=27 |
| Geometric Mean (95% CI) | 4.14 (3.96, 4.34) | 4.1 (3.9, 4.4) | 4.1 (3.8, 4.5) | 3.3 (2.6, 4.2) | 5.5 (4.8, 6.5) |
| Median (IQR) | 4.24 (3.08, 5.52) | 4.2 (3.0, 5.7) | 4.2 (3.0, 5.3) | 3.8 (2.3, 4.3) | 5.2 (4.2, 7.4) |
| B1B cells | n=449 | n=246 | n=157 | n=19 | n=27 |
| Geometric Mean (95% CI) | 1.02 (0.97, 1.08) | 1.04 (0.96, 1.12) | 0.96 (0.87, 1.06) | 0.96 (0.69, 1.34) | 1.4 (1.1, 1.7) |
| Median (IQR) | 1.08 (0.77, 1.5) | 1.10 (0.77, 1.50) | 1.00 (0.75, 1.40) | 0.95 (0.55, 1.40) | 1.5 (1.2, 1.9) |
| Adaptive immune markers |  |  |  |  |  |
| T lymphocytes  | n=451 | n=247 | n=157 | n=20 | n=27 |
| Geometric Mean (95% CI) | 14.8 (14.2, 15.4) | 14.1 (13.4, 14.8) | 15.7 (14.6, 16.8) | 17.9 (15.4, 20.9) | 14.9 (12.7, 17.6) |
| Median (IQR) | 15.4 (11.5, 20.0) | 14.6 (10.9, 19.0) | 16.2 (12.4, 21.0) | 18.3 (13.4, 23.9) | 15.4 (11.2, 20.2) |
| CD4+ T cells | n=450 | n=247 | n=156 | n=20 | n=27 |
| Geometric Mean (95% CI) | 10.0 (9.6, 10.5) | 9.6 (9.1, 10.1) | 10.6 (9.8, 11.4) | 12.1 (11.3, 15.1) | 9.5 (8.0, 11.4) |
| Median (IQR) | 10.4 (7.7, 13.7) | 10.1 (7.3, 12.9) | 11.0 (8.4, 14.4) | 14.7 (9.5, 16.1) | 9.8 (6.8, 12.3) |
| Naive CD4+ T cells  | n=448 | n=246 | n=155 | n=20 | n=27 |
| Geometric Mean (95% CI) | 96.5 (96.4, 96.7)  | 96.6 (96.3, 96.8) | 97 (96, 97) | 96 (96, 97) | 96.6 (96.0, 97.2) |
| Median (IQR)  | 97.0 (96.0, 98.0) | 97.0 (96.0, 98.0) | 97.0 (95.0, 98.0) | 96.0 (95.0, 97.0) | 96.4 (95.0, 98.0) |
| T regulatory cells | n=449 | n=247 | n=155 | n=20 | n=27 |
| Geometric Mean (95% CI) | 1.14 (1.09, 1.19) | 1.1 (1.0, 1.2) | 1.17 (1.09, 1.25) | 1.48 (1.18 , 1.86) | 1.0 (0.9, 1.2) |
| Median (IQR)  | 1.14 (0.89, 1.55) | 1.1 (0.9, 1.5) | 1.18 (0.89, 1.60) | 1.33 (1.06 , 1.74) | 1.0 (0.8, 1.3) |
| CD8+ T cells  | n=447 | n=245 | n=155 | n=20 | n=27 |
| Geometric Mean (95% CI) | 4.98 (4.78, 5.19) | 4.8 (4.5, 5.0) | 5.3 (4.9, 5.6) | 5.6 (4.7 , 6.8) | 5.1 (4.3, 6.1) |
| Median (IQR)  | 5.0 (3.78, 6.7) | 4.8 (3.5, 6.5) | 5.2 (4.1, 6.7) | 5.7 (4.2 , 7.4) | 5.9 (3.7, 7.2) |
| Naïve CD8+ T cells | n=447 | n=245 | n=155 | n=20 | n=27 |
| Geometric Mean (95% CI) | 91.1 (90.8, 93.4) | 91.7 (91.1, 92.4) | 91 (91, 92) | 90 (86, 93) | 91.2 (89.1, 93.4) |
| Median (IQR) | 93 (89.3, 95.1) | 93.0 (90.0, 95.1) | 93 (89, 95) | 92 (89, 95) | 93.2 (89.0, 95.0) |
| B lymphocytes | n=449 | n=246 | n=157 | n=19 | n=27 |
| Geometric Mean (95% CI) | 2.7 (2.6, 2.9) | 2.6 (2.4, 2.8) | 2.8 (2.6, 3.1) | 3.3 (2.4, 4.6) | 3.1 (2.5, 3.9) |
| Median (IQR) | 2.8 (2.0, 4.1) | 2.7 (2.0, 3.9) | 2.9 (2.0, 4.3) | 3.5 (2.4, 5.9) | 3.1 (2.0, 5.1) |
| Naïve B cells | n=449 | n=246 | n=157 | n=19 | n=27 |
| Geometric Mean (95% CI) | 96.6 (96.4, 96.8) | 96.6 (96.3, 96.9) | 97 (97, 97) | 97 (96, 97) | 95.0 (94.0, 96.0) |
| Median (IQR) | 97.0 (95.7, 98.0) | 97.0 (96.0, 98.0) | 97 (96, 98) | 97 (95, 98) | 95.7 (93.5, 96.8) |
| CD10+ Naïve B cells | n=440 | n=240 | n=155 | n=19 | n=26 |
| Geometric Mean (95% CI) | 23.6 (22.8, 24.4) | 23.6 (22.5, 24.7) | 24 (22, 25) | 27 (23, 32) | 21.2 (18.6, 24.2) |
| Median (IQR) | 23.5 (19.1, 30.5) | 24.0 (18.9, 30.8) | 23 (19, 31) | 26 (20, 34) | 22.6 (17.7, 27.1) |

*a* All immune marker variables have been log transformed

SGA, small for gestational age (birth weight below the 10th centile or 2SD below mean for GA of reference/normal birth curves); AGA, appropriate for gestational age (birth weight between the 10th and 90th centile for GA of reference/normal birth curves); ERC,exponentiated regression coefficient, ordinary least square (OLS) regression analysis after log transformation of dependent variable (immune marker); 95% CI, 95 percent confidence interval.