## **Table 1. Clinical and demographic characteristics of the study population\*.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Banjul | Blantyre | Kilifi | Kumasi | Lambaréné | Libreville |
|  | N = 3,318 | N = 5,358 | N = 6,846 | N = 6,925 | N = 1,784 | N = 1,662 |
| Age, median (Q1, Q3), months | 32 (18, 51) | 26 (14, 46) | 26 (14, 43) | 24 (12, 42) | 28 (16, 56) | 25 (15, 42) |
| Sex, N (%) Female | 1,617 (48) | 2,493 (46) | 3,188 (46) | 3,113 (45) | 841 (47) | 793 (47 |
| Weight, median (Q1, Q3), kg | 11·0  (9·0, 15·0) | 10·2  (8·4, 13·5) | 9·9  (8·0, 12·6) | 10·0  (8·0, 13·5) | 11·0  (9·0, 15·0) | 11·0  (9·0, 14·0) |
| Weight-for-age, median (Q1, Q3), Z-score | -1·36  (-2·30, -0·50) | -1·22  (-2·19, -0·35) | -1·7  (-2·56, -0·86) | -1·15  (-2·04, -0·35) | -1·01  (-1·84, -0·19) | -0·08  (-1·70, 0·05) |
| Temperature, median (Q1, Q3), °C | 37·7  (37·1, 38·6) | 38·5  (37·8, 39·2) | 38·3  (37·3, 39·2) | 37·8  (37·0, 38·6) | 38·5  (37·7, 39·5) | 38·6  (37·9, 39·5) |
| Respirations, median (Q1, Q3), min-1 | 34 (28, 44) | 38 (36, 44) | 36 (30, 46) | 42 (36, 54) | 40 (32, 48) | 42 (36, 52) |
| Respiratory Distress†, N (%) | 692 (20) | 473 (9) | 1,563 (23) | 1,631 (24) | 99 (6) | 212 (12·5) |
| Haemoglobin, median (Q1, Q3), g/L | 63 (45, 86) | 88 (68, 103) | 80 (61, 96) | 62 (47, 85) | 77 (58, 95) | 62 (46, 84) |
| Severe anaemia‡, N (%) | 640 (19) | 282 (5) | 489 (7) | 999 (14) | 131 (7) | 262 (15·4) |
| Glucose, median (Q1, Q3), mmol/L | 6·4 (4·8, 8·0) | 5·3 (4·4, 6·2) | 5·2 (4·2, 6·3) | 5·1 (4·2, 6·1) | 4·1 (3·1, 5·1) | 5·3 (4·3, 6·4) |
| Hypoglycemia§, N (%) | 126 (6) | 134 (3) | 322 (5) | 295 (4) | 164 (10) | 53 (3) |
| Parasitaemia, median (Q1, Q3), ul-1 \*\* | 19,500  (1,500-78,000) | 83,778  (33,333-189,111) | 39,330  (3,140-215,800) | 65,877  (14,281-241,152) | 51,000  (9,000-200,000) | 71,500  (15,500-220,000) |
| Blantyre Coma Score, N (%) |  |  |  |  |  |  |
| 5 | 2,587 (76) | 4,809 (90) | 5,539 (80) | 5,289(76) | 1,587 (89) | 1,128 (67) |
| 4 | 248 (7) | 113 (2) | 468 (7) | 464 (7) | 55 (3) | 219 (13) |
| 3 | 275 (8) | 147 (3) | 187 (3) | 350 (5) | 56 (3) | 155 (9) |
| 2 | 184 (5) | 128 (2) | 364 (5) | 422 (6) | 64 (4) | 127 (8) |
| 1 | 70 (2) | 85 (2) | 172 (3) | 238 (3) | 27 (2) | 51 (3) |
| 0 | 31 (1) | 81 (2) | 179 (3) | 178 (3) | 1 (0·1) | 16 (1) |
| Impaired consciousness‖, N (%) | 808 (24) | 554 (10) | 1,370 (20) | 1,652 (24) | 203 (11) | 568 (33) |
| Lactate, median (Q1, Q3), mmol/L | 3·9 (2·4,7·0) | 3·6 (2·2,6·0) | 2·3 (1·6,3·5) | 3·2 (2·1,5·2) | 3·8 (2·4,5·3) | 3·8 (2·4,5·8) |
| Lactate, N (%) |  |  |  |  |  |  |
| < 3·0 mmol/L | 990 (35) | 2,108 (40) | 4,517 (67) | 3,104 (45) | 495 (35) | 503 (35) |
| 3·0 - 4·9 mmol/L | 768 (27) | 1,400 (27) | 1,351 (20) | 1,954 (28) | 520 (37) | 469 (33) |
| ≥ 5·0 mmol/L | 1,106 (39) | 1,737 (33) | 866 (13) | 1,886 (27) | 408 (29) | 453 (32) |
| Transfused¶, N (%) | 1,526 (46) | 813 (15) | 1,029 (15) | 3,934 (57) | 382 (21) | 829 (50) |
| Outcome |  |  |  |  |  |  |
| Survived, N | 3,012 | 5,148 | 6,640 | 6,596 | 1,759 | 1,599 |
| Died, N (%) | 316 (7) | 133 (3) | 232 (3) | 313 (5) | 24 (1) | 83 (5) |
| Absconded, N | 24 | 82 | 30 | 35 | 9 | 18 |

\* Variables were compared across sites using Kruskal-Wallis test for continuous variables, and chi-squared for categorical variables. All variables differed significantly between sites (P< 0·0001), except sex (P = 0·12).

† Respiratory distress: presence of deep breathing, irregular breathing, or chest indrawing.

‡ Severe anemia: hemoglobin less than or equal to 40 g/L.

§ Hypoglycaemia: blood glucose less than 2·2 mmol/L

‖ Impaired consciousness: Blantyre Coma Score less than or equal to 4.

¶ Baseline data separated by transfusion status is available in Table S1.

\*\* In Blantyre and Kumasi, parasite density was counted per 200 WBCs and an assumption of 8,000 WBC per microliter was applied. In Kilifi, the parasite count was calculated by multiplying the parasite count per 100 WBC times the WCC determined by Coulter counter (Coulter MDII). At all other sites, parasite density was based on reading 100 high-powered fields. Complete blood counts were not available. This approach may have introduced variability in the estimation of parasite density that may have varied by site.

The percentage of missing values for each variable were as follows: age (0%), sex (0%), weight (0%), temperature (0·2%), respirations (0·4%), respiratory distress (0·1%), haemoglobin (0·3%), severe anaemia (0·3%), glucose (5·9%), hypoglycaemia (5·9%), parasitaemia (0%), Blantyre coma score (0·1%), Impaired consciousness (0·1%), lactate (5·6%), transfused (0·8%), outcome (0·2%).

**Table 2. Association of blood transfusion with death in site- and severity-adjusted analyses.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | | **OR** | **(95% CI)** | **LRT P\*** |
| ***Site-Only Adjusted Analysis (N = 25,738)*†** | |  |  |  |
| **Transfusion** | | 0·82 | (0·71, 0·94) | p = 0·0030 |
| **Study site** | |  |  | < 0·0001 |
|  | | *c-statistic of the fitted model = 0·64* | | |
| ***Site and Severity Adjusted Analysis (N = 22,986)*‡** | |  |  |  |
| **Transfusion** | | 0·50 | (0·42, 0·60) | < 0·0001 |
| **Age**§ | | 1·03 | (1·01, 1·04) | < 0·0001 |
| **Temperature, ᵒC** | | 0·83 | (0·78, 0·88) | < 0·0001 |
| **Parasite density, ln (parasites/µl of blood)** | | 0·78 | (0·73, 0·84) | < 0·0001 |
| **Lactate, mmol/L** | |  |  | < 0·0001 |
|  | **< 3·0** | — | — |  |
|  | **3·0 - 4·9** | 1·43 | (1·14, 1·78) |  |
|  | **≥ 5·0** | 3·22 | (2·64, 3·93) |  |
| **Severe anaemia** | | 1·28 | (1·04, 1·57) | 0·028 |
| **Impaired consciousness** | | 4·00 | (3·43, 4·68) | < 0·0001 |
| **Respiratory distress** | | 3·63 | (3·10, 4·27) | < 0·0001 |
| **Hypoglycaemia** | | 3·44 | (2·82, 4·20) | < 0·0001 |
| **Study site** | |  |  | < 0·0001 |
|  | | *c-statistic of the fitted model = 0·85* | | |

OR, odds ratio; LRT, likelihood ratio test; CI, confidence interval; BCS, Blantyre comma score; *c-statistics*, area under the receiver operating characteristic curve of the predicted proportions by the model.

\*P-value of the likelihood ratio test comparing the reduced model (with the corresponding predictor deleted from the model) with the full model.

**†**The crude odds ratio (95% CI) for death and blood transfusion in analysis ignoring study site and including all 25,738 children with information for transfusion and death was 1·09 (0·96, 1·23; P = 0·20). The odds ratio (95% CI) for blood transfusion in analysis adjusting only for study site when analyzing only the 22,986 children with information available for all covariates in the adjusted model was 0·86 (0·75, 1·01; P = 0·07).

**‡** Sex was not statistically significant in crude analysis, analysis adjusting by site, analysis including transfusion, and in any of the two selected final models. Exclusion of sex did not affect the OR of transfusion, did not increase the AUC-ROC, and did not decrease the AIC and BIC. In the adjusted model of this table, the OR (95% CI) for male (vs. female) sex and death was 0·96 (0·83, 1·10; P = 0·54). Fully adjusted OR (95% CI) for death by site using Banjul as a reference site: Blantyre, Malawi 0·33 (0·25, 0·43); Lambaréné, Gabon 0·57 (0·41, 0·78); Libreville, Gabon 0·15 (0·08, 0·25); Kilifi, Kenya 0·33 (0·26, 0·42); Kumasi, Ghana 0·43 (0·35, 0·54).

§The OR for age is per 6 months change.