**Supplementary Materials**

***Supplementary Methods***

*Definitions of Meningitis and Encephalitis*

CSF pleocytosis: A raised CSF WBC count (CSF pleocytosis) was defined as age 0-28 days CSF WBC ≥20 X106/L, age >28 days CSF WBC >5 X106/L. The CSF white blood cell (WBC) count was corrected for red blood cell count at a ratio of 500X106/L RBC:1 X106/L WBC.

Definite bacterial meningitis: Bacterial pathogen in CSF, or raised CSF WBC and relevant pathogen present in blood on culture or PCR, or CSF gram stain positive and corresponding pathogen present in blood. Relevant pathogens in blood included *N. meningitidis, S. pneumoniae, H. influenzae,* Group B Streptococcus, *E. coli*, *S. aureus* and Group A Streptococcus.

The following organisms were defined as contaminants in CSF or blood cultures unless treated as a pathogen by the clinical team: coagulase-negative staphylococci, diptheroids, micrococci, bacillus species, corynebacterium, alpha haemolytic Streptococci, *Pseudomonas oryzihchitens*, *Pantoea dispersa*, *Kocuria* species, *Moraxella osloensis*, *Granulicatella elegans*, *Neisseria elongata*, and *Proprionibacterium acnes*.

Probable bacterial meningitis: Raised CSF WBC and pure growth of bacterial pathogen in urine.

Aseptic meningitis: Raised CSF WBC and no bacterial pathogen identified. Aseptic meningitis includes atypical organisms, and any non-bacterial cause identified.

Definite viral meningitis: Raised CSF WBC and viral pathogen found in CSF or blood; or enterovirus, parechovirus or HSV present in CSF with a raised or normal CSF WBC.

Probable viral meningitis: Raised CSF WBC, and enterovirus or parechovirus in stool.

Aseptic meningitis with unknown aetiology: Raised CSF WBC and no causative pathogen identified.

Possible meningitis: Pathogen known to cause bacterial meningitis in blood and no evaluable LP result, or pathogen of uncertain significance in CSF and either no available or no raised CSF WBC, or discharge diagnosis of meningitis but with no other features of confirmed or probable meningitis.

Meningoencephalitis: Meningitis as previously defined and discharge diagnosis of encephalitis or meningoencephalitis.

Possible encephalitis: No raised or no available CSF WBC, and discharge diagnosis of encephalitis.

Definite encephalitis cases were not defined for this analysis because of incomplete neuroimaging and neurophysiology data, which are required for the encephalitis international consensus case definition.26

### Development of a new multivariable rule to predict probability of bacterial meningitis

Two sets of potential predictors were pre-specified before data analysis for both rules (Supplementary Table 1). The predictors with more than 50% missing data in the corresponding population were first excluded, because these predictors are unlikely to be clinically useful given the challenge to collect them. To account for the missing data, multiple imputation by chained equations was used to generate 10 imputed datasets, assuming the data were missing at random. For each of the datasets, we constructed 500 bootstrap samples by randomly sampling with replacement. The lasso selection with 1 standard error penalty was applied to each of the 500 bootstrap samples to develop 500 models, as this method was approved to have good performance in predictor selection.27 The inclusion frequency of a variable was calculated as the proportion of the variable appearing in the 500 models.28 This means each variable has 10 inclusion frequencies (one for each imputed dataset). We selected the predictors with a median inclusion frequency >75% among the 10 imputed datasets as the final predictor panel.29 This process was conducted separately in study participants for the pre-LP rule and in those with CSF pleocytosis for the post-LP rule.

The performance of the two sets of pre-LP and post-LP clinical rules were evaluated by the calibration and the area under the receiver operating characteristic curve (AUROC). The 10 imputed datasets were appended and 100 bootstrap samples from the combined dataset were drawn. For each of the bootstrap samples, a logistic regression model was fitted using the selected predictors. The model was applied in the original dataset to predict the probability of bacterial meningitis. The mean predicted probability derived from the 100 bootstrap samples was calculated, and compared with the observed bacterial meningitis frequencies in the original dataset, by dividing the dataset into 20 risk groups of equal size according to the mean predicted probability.30 The mean predicted probability was also used to plot the ROC curve, and the AUROC was reported.

To develop a ‘points scoring system’ for clinical use, continuous variables among the selected pre-LP and post-LP predictors were dichotomised by a cut-off to maximise accuracy in distinguishing participants with and without bacterial meningitis. Two logistic regression models, based on the categorised pre-LP and post-LP predictors, were developed. The pre-LP and post-LP points score system were derived by rounding the coefficients from the logistic regression models to the nearest 0·5.

***Supplementary Figure 1. Causes of hospitalisation in children without meningitis or encephalitis (controls)***



***Supplementary Figure 2. Calibration plots for (a) post-LP rule, children with CSF pleocytosis and (b) pre-LP rule (all children)***

***(a)***



**(b)**



***Supplementary Figure 3. Receiver operating characteristic curves for (a) post-LP rule, children with CSF pleocyosis (AUROC=0·91) and (b) pre-LP rule, all children (AUROC=0·87)***

***(a)***



**(b)**



***Supplementary Table 1. Variables considered for prediction models of bacterial meningitis.***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Symptoms on admission** | **Type** | **Pre-LP rule** | **Post-LP rule** | **% missing in all children** | **% missing in children with CSF pleocytosis** |
| **Clinical symptoms at admission** |  |  |  |  |  |
| History of Fever | Binary: Y/N | × | × | 1·0% | 0·7% |
| Respiratory symptoms | Binary: Y/N | × | × | 1·7% | 2·0% |
| Rash | Binary: Y/N | × | × | 2·8% | 2·4% |
| Vomiting | Binary: Y/N | × | × | 2·2% | 1·9% |
| Diarrhoea | Binary: Y/N | × | × | 3·1% | 3·0% |
| Headache | Binary: Y/N | × | × | 42·8% | 40·7% |
| Seizures in last 24 hours | Binary: Y/N | × | × | 2·3% | 2·4% |
| Seizures >24 hours | Binary: Y/N | × | × | 8·6% | 8·4% |
| Neck stiffness | Binary: Y/N | × | × | 25·8% | 23·8% |
| Neck pain | Binary: Y/N | × | × | 37·0% | 33·8% |
| Altered consciousness | Binary: Y/N | × | × | 6·4% | 5·5% |
|  |  |  |  |  |  |
| **Examination on admission** |  |  |  |  |  |
| Temperature(◦C) | Continuous | × | × | 3·2% | 3·4% |
| Heart rate(/min) | Continuous | × | × | 2·6% | 2·5% |
| Respiratory rate(/min) | Continuous | × | × | 4·9% | 4·4% |
| Prolonged capillary refill time | Binary: Y/N | × | × | 48·8% | 50·1% |
| Respiratory signs | Binary: Y/N | × | × | 3·0% | 3·0% |
| Photophobia | Binary: Y/N | × | × | 57·5% | 58·1% |
| Neck stiffness | Binary: Y/N | × | × | 53·2% | 53·3% |
| Kernig’s sign | Binary: Y/N | × | × | 79·0% | 79·2% |
| Brudzunski’s sign | Binary: Y/N | × | × | 81·5% | 81·9% |
| Rash | Categorical: Absent; Non-blanching; Other  | × | × | 9·8% | 10·1% |
| Fontanelle bulging | Binary: Y/N | × | × | 49·5% | 52·3% |
| GCS<15 | Binary: Y/N | × | × | 65·3% | 61·5% |
|  |  |  |  |  |  |
| **Blood parameters** |  |  |  |  |  |
| Blood WBC count (X109/L) | Continuous | × | × | 2·0% | 1·1% |
| Blood neutrophil count (X109/L) | Continuous | × | × | 2·4% | 1·5% |
| Blood lymphocyte count (X109/L) | Continuous | × | × | 3·3% | 2·6% |
| Blood CRP (mg/L) | Categorical: <5; 5-<15; 15-<40; 40-<100; ≥100 | × | × | 2·9% | 1·6% |
|  |  |  |  |  |  |
| **CSF parameters** |  |  |  |  |  |
| CSF glucose (mmol/L) | Continuous |  | × |  | 8·5% |
| CSF:plasma glucose ratio | Continuous |  | × |  | 56·1% |
| Corrected CSF WBC count (X106/L)\* | Continuous |  | × |  | 2·5% |
| CSF neutrophil number (X106/L) | Continuous |  | × |  | 30·8% |
| CSF lymphocyte number (X106/L) | Continuous |  | × |  | 30·8% |
| CSF protein (g/L) | Continuous |  | × |  | 12·4% |

\* Corrected for red blood cell count at a ratio of 500X106/L RBC:1X106/L WBC

The variables with >50% missing data are highlighted in grey, and the predictors in the final rules are heighted in green.

***Supplementary Table 2: Causes of death in study participants***

|  |  |  |
| --- | --- | --- |
| **Age group** | **Sex** | **Diagnosis** |
|  |  |  |
| **MENINGITIS** |  |  |
| 10-16 years | F | Bacterial meningitis – *Streptococcus pneumoniae* |
| 29 days to <3 months | F | Viral meningitis -enterovirus |
| 10-16 years | F | Aseptic meningitis – aetiology unknown |
|  |  |  |
| **NOT MENINGITIS** |  |  |
| 0-28 days | F | Disseminated HSV-2 infection |
| 29 days to <3 months | F | Leigh’s encephalopathy |
| 29 days to <3 months | M | Menke’s kinky hair syndrome |
| 6-11 months | F | Neurodegenerative disorder (unspecified) |
| 12-23 months | M | Leukoencephalopathy |
| 2-4 years | F | Status epilepticus |
| 2-4 years | F | Ornithine transcarbamylase deficiency |
| 5-9 years | F | Acute lower respiratory tract infection |
| 10-16 years | F | Epilepsy |

***Supplementary Table 3. Causes of hospitalisation in children without meningitis or encephalitis (controls)***

| **Control group** | **Age groups** |
| --- | --- |
| **0-28 days** | **29 days to** **< 3 months** | **3-5 months** | **6-11 months** | **12-23 months** | **2-4 years** | **5-9 years** | **10-16 years** | **Total** |
| **Total n** | 454 | 644 | 227 | 138 | 167 | 98 | 94 | 79 | 1901 |
|  |  |  |  |  |  |  |  |  |  |
| **INFECTION** | **363** | **586** | **202** | **114** | **115** | **52** | **27** | **17** | **1476** |
| Suspected sepsis, n  | 143  | 163  | 39  | 19  | 9  | 2  | 3  | 4  | 382  |
| Non-specific viral illness, n  | 63  | 130  | 53  | 21  | 16  | 10  | 11  | 6  | 310  |
| Urinary tract infection, n  | 77  | 122  | 47  | 13  | 8  | 3  | 3  | 2  | 275  |
| Bronchiolitis, n  | 29  | 47  | 10  | 2  | 1  | 1  | 0 | 0 | 90  |
| Other lower respiratory tract infection, n  | 11  | 26  | 16  | 9  | 15  | 6  | 3  | 1  | 87  |
| Febrile seizure secondary to infection, n  | 1  | 0 | 6  | 25  | 39  | 10  | 4  | 0 | 85  |
| Febrile illness – not otherwise specified, n  | 13  | 40  | 13  | 4  | 8  | 5  | 2  | 0 | 85  |
| Upper respiratory tract infection, n  | 6  | 26  | 3  | 11  | 7  | 2  | 0 | 2  | 57  |
| Gastroenteritis, n  | 4  | 19  | 7  | 5  | 9  | 7  | 0 | 0 | 51  |
| Bacteraemia, n  | 8  | 10  | 7  | 3  | 1  | 4  | 0 | 1  | 34  |
| Other viral infection without meningitis (EV, VZV, HSV, HHV06) | 8 | 3 | 1 | 2 | 2 | 2 | 1  | 1 | 20 |
|  |  |  |  |  |  |  |  |  |  |
| **NEUROLOGICAL DISORDER** | **0** | **0** | **0** | **2** | **10** | **3** | **11** | **9** | **35** |
| Seizure (not febrile seizure), n  | 0 | 0 | 0 | 2  | 9  | 0 | 2  | 0 | 13  |
| Headache/migraine, n  | 0 | 0 | 0 | 0 | 0 | 1  | 4  | 6  | 11  |
| Guillain Barre syndrome, n  | 0 | 0 | 0 | 0 | 0 | 2  | 1  | 1  | 4  |
| Transverse myelitis, n  | 0 | 0 | 0 | 0 | 1  | 0 | 1  | 1  | 3  |
| Idiopathic Intercranial hypertension, n  | 0 | 0 | 0 | 0 | 0 | 0 | 1  | 1  | 2  |
| Optic neuritis, n  | 0 | 0 | 0 | 0 | 0 | 0 | 2  | 0 | 2  |
|  |  |  |  |  |  |  |  |  |  |
| **OTHER** | **4** | **7** | **7** | **3** | **6** | **7** | **5** | **13** | **52** |
| Other acute illness not specified, n  | 4  | 6  | 4  | 0 | 5  | 5  | 2  | 13  | 39  |
| Kawasaki Disease, n  | 0 | 0 | 3  | 3  | 1  | 2  | 3  | 0 | 12  |
| Surgical disorder, n  | 0 | 1  | 0 | 0 | 0 | 0 | 0 | 0 | 1  |
|  |  |  |  |  |  |  |  |  |  |
| **UNKNOWN** | **87** | **51** | **18** | **19** | **36** | **36** | **51** | **40** | **338** |

***Supplementary Table 4. Clinical signs and symptoms in children aged 0-28 days with suspected meningitis***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Any bacterial meningitis | All aseptic meningitis | Possible meningitis | Control |
|  | N=35 | N=177 | N=22 | N=454 |
| Duration of symptoms prior to hospital presentation (median, IQR) | 1·0 (0·0-2·0) [n=34] | 1·0 (0·0-2·0) [n=176] | 1·0 (0·0-1·8) [n=22] | 1·0 (0·0-2·0) [n=449] |
| **SYMPTOMS** |  |  |  |  |
| Fever | 16/33 (45·7%) | 135/177 (76·3%) | 9/22 (40·9%) | 195/451 (43·0%) |
| Any respiratory symptoms\* | 18/34 (51·4%) | 85/177 (48·0%) | 13/22 (59·1%) | 210/454 (46·3%) |
| Rash | 2/34 (5·7%) | 28/177 (15·8%) | 2/22 (9·1%) | 59/446 (13·0%) |
| Vomiting | 11/32 (31·4%) | 34/176 (19·2%) | 2/22 (9·1%) | 126/446 (27·8%) |
| Diarrhoea | 4/33 (11·4%) | 16/176 (9·0%) | 3/21 (13·6%) | 49/442 (10·8%) |
| Seizures within 24 hours before admission | 5/33 (14·3%) | 2/173 (1·1%) | 1/20 (4·5%) | 13/446 (2·9%) |
| Seizures outside 24 hours before admission | 2/30 (5·7%) | 3/157 (1·7%) | 1/18 (4·5%) | 3/420 (0·7%) |
| Neck stiffness | 0/24 (0·0%) | 5/126 (2·8%) | 0/18 (0·0%) | 4/331 (0·9%) |
| Neck pain | 0/21 (0·0%) | 5/104 (2·8%) | 0/15 (0·0%) | 5/266 (1·1%) |
| Altered consciousness\*\* | 10/32 (28·6%) | 31/165 (17·5%) | 9/21 (40·9%) | 105/429 (23·1%) |
| **SIGNS ON ADMISSION** |  |  |  |  |
| Temperature | 38·3 (37·4-39·0) [n=34] | 38·5 (38·0-39·0) [n=174] | 37·8 (37·4-38·2) [n=21] | 37·5 (37·1-38·4) [n=444] |
| Heart rate (/min) | 162·0 (138·8-185·2) [n=34] | 166·0 (152·0-182·0) [n=173] | 161·5 (144·0-191·0) [n=20] | 155·0 (136·8-175·2) [n=448] |
| Respiratory rate (/min) | 48·0 (40·0-56·5) [n=32] | 46·0 (40·0-55·0) [n=173] | 49·0 (42·0-60·0) [n=19] | 44·0 (38·0-52·0) [n=441] |
| Prolonged central capillary refill time | 3/23 (8·6%) | 15/96 (8·5%) | 4/10 (18·2%) | 43/245 (9·5%) |
| Respiratory signs | 10/34 (28·6%) | 45/174 (25·4%) | 7/21 (31·8%) | 137/448 (30·2%) |
| Photophobia | 0/9 (0·0%) | 0/61 (0·0%) | 0/5 (0·0%) | 1/165 (0·2%) |
| Neck stiffness | 0/7 (0·0%) | 3/75 (1·7%) | 0/5 (0·0%) | 0/196 (0·0%) |
| Kernig’s sign positive | 0/3 (0·0%) | 0/33 (0·0%) | 0/1 (0·0%) | 0/87 (0·0%) |
| Brudzinski’s sign positive | 0/2 (0·0%) | 0/32 (0·0%) | 0/1 (0·0%) | 0/84 (0·0%) |
| Rash |  |  |  |  |
| *Absent* | 23 (65·7%) | 126 (71·2%) | 17 (77·3%) | 327 (72·0%) |
| *Non-blanching* | 1 (2·9%) | 6 (3·4%) | 1 (4·5%) | 9 (2·0%) |
| *Other* | 3 (8·6%) | 27 (15·3%) | 1 (4·5%) | 67 (14·8%) |
| *Missing* | 8 (22·9%) | 18 (10·2%) | 3 (13·6%) | 51 (11·2%) |
| Fontanelle bulging (if open fontanelle) | 9/27 (25·7%) | 4/130 (2·3%) | 2/14 (9·1%) | 5/326 (1·1%) |
| GCS | 15·0 (15·0-15·0) [n=6] | 15·0 (15·0-15·0) [n=40] | 15·0 (14·2-15·0) [n=4] | 15·0 (15·0-15·0) [n=105] |

\* Including fast breathing, indrawing, grunting, apnoea, coryza, sore throat, cough, wheeze

\*\* Including drowsiness or coma

***Supplementary Table 5. Clinical signs and symptoms in children aged between 29 days and <3 months with suspected meningitis***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Any bacterial meningitis | All aseptic meningitis | Possible meningitis | Control |
|  | N=49 | N=288 | N=15 | N=644 |
| Duration of symptoms prior to hospital presentation (median, IQR) | 1·0 (0·0-2·0) [n=49] | 1·0 (0·0-2·0) [n=285] | 2·0 (1·0-3·5) [n=15] | 1·0 (0·0-2·0) [n=639] |
| **SYMPTOMS** |  |  |  |  |
| Fever | 39/49 (79·6%) | 246/288 (85·4%) | 8/15 (53·3%) | 472/641 (73·3%) |
| Any respiratory symptoms\* | 26/48 (53·1%) | 116/283 (40·3%) | 12/15 (80·0%) | 337/636 (52·3%) |
| Rash | 5/49 (10·2%) | 75/284 (26·0%) | 5/15 (33·3%) | 139/625 (21·6%) |
| Vomiting | 21/47 (42·9%) | 85/284 (29·5%) | 3/15 (20·0%) | 198/629 (30·7%) |
| Diarrhoea | 8/47 (16·3%) | 52/280 (18·1%) | 1/15 (6·7%) | 100/627 (15·5%) |
| Seizures within 24 hours before admission | 2/46 (4·1%) | 8/283 (2·8%) | 2/15 (13·3%) | 19/628 (3·0%) |
| Seizures outside 24 hours before admission | 0/44 (0·0%) | 2/258 (0·7%) | 0/14 (0·0%) | 4/591 (0·6%) |
| Neck stiffness | 0/37 (0·0%) | 10/218 (3·5%) | 0/10 (0·0%) | 6/431 (0·9%) |
| Neck pain | 2/34 (4·1%) | 10/174 (3·5%) | 0/7 (0·0%) | 5/361 (0·8%) |
| Altered consciousness\*\* | 12/46 (24·5%) | 57/269 (19·8%) | 2/14 (13·3%) | 116/603 (18·0%) |
| **SIGNS ON ADMISSION** |  |  |  |  |
| Temperature | 38·3 (37·7-39·0) [n=47] | 38·5 (38·0-39·0) [n=285] | 37·8 (37·2-38·2) [n=14] | 38·1 (37·5-38·6) [n=636] |
| Heart rate (/min) | 170·0 (160·5-194·0) [n=47] | 170·0 (155·0-186·2) [n=284] | 172·0 (143·5-181·0) [n=15] | 167·5 (152·0-180·0) [n=636] |
| Respiratory rate (/min) | 47·0 (42·0-55·0) [n=47] | 46·0 (40·0-52·0) [n=276] | 50·0 (40·5-58·0) [n=15] | 44·0 (39·0-52·0) [n=623] |
| Prolonged central capillary refill time | 9/28 (18·4%) | 21/164 (7·3%) | 2/9 (13·3%) | 68/362 (10·6%) |
| Respiratory signs | 19/46 (38·8%) | 66/283 (22·9%) | 6/15 (40·0%) | 179/635 (27·8%) |
| Photophobia | 0/18 (0·0%) | 2/106 (0·7%) | 0/6 (0·0%) | 4/243 (0·6%) |
| Neck stiffness | 0/19 (0·0%) | 5/120 (1·7%) | 0/5 (0·0%) | 3/271 (0·5%) |
| Kernig’s sign positive | 0/7 (0·0%) | 1/55 (0·3%) | 1/5 (6·7%) | 0/118 (0·0%) |
| Brudzu=inski’s sign positive | 0/7 (0·0%) | 0/54 (0·0%) | 0/4 (0·0%) | 0/114 (0·0%) |
| Rash |  |  |  |  |
| *Absent* | 37 (75·5%) | 159 (55·2%) | 9 (60·0%) | 422 (65·5%) |
| *Non-blanching* | 1 (2·0%) | 27 (9·4%) | 3 (20·0%) | 49 (7·6%) |
| *Other* | 5 (10·2%) | 86 (29·9%) | 2 (13·3%) | 117 (18·2%) |
| *Missing* | 6 (12·2%) | 16 (5·6%) | 1 (6·7%) | 56 (8·7%) |
| Fontanelle bulging (if open fontanelle) | 8/30 (16·3%) | 11/197 (3·8%) | 1/10 (6·7%) | 15/430 (2·3%) |
| GCS | 15·0 (15·0-15·0) [n=14] | 15·0 (15·0-15·0) [n=68] | 15·0 (15·0-15·0) [n=5] | 15·0 (15·0-15·0) [n=144] |

\* Including fast breathing, indrawing, grunting, apnoea, coryza, sore throat, cough, wheeze

\*\* Including drowsiness or coma

***Supplementary Table 6. Clinical signs and symptoms in children aged between 3 months and 11 months with suspected meningitis***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Any bacterial meningitis | All aseptic meningitis | Possible meningitis | Control |
|  | N=61 | N=103 | N=25 | N=365 |
| Duration of symptoms prior to hospital presentation, days (median, IQR) | 3·0 (1·0-4·5) [n=59] | 2·0 (1·0-4·0) [n=100] | 2·0 (1·0-4·2) [n=24] | 2·0 (1·0-3·0) [n=359] |
| **SYMPTOMS** |  |  |  |  |
| Fever | 56/60 (91·8%) | 87/103 (84·5%) | 21/23 (84·0%) | 305/359 (83·6%) |
| Any respiratory symptoms\* | 39/59 (63·9%) | 43/101 (41·7%) | 16/24 (64·0%) | 202/357 (55·3%) |
| Rash | 17/58 (27·9%) | 34/101 (33·0%) | 13/24 (52·0%) | 70/353 (19·2%) |
| Vomiting | 37/58 (60·7%) | 48/101 (46·6%) | 8/24 (32·0%) | 143/357 (39·2%) |
| Diarrhoea | 15/58 (24·6%) | 21/101 (20·4%) | 9/22 (36·0%) | 87/354 (23·8%) |
| Headache | 7/34 (11·5%) | 5/48 (4·9%) | 1/15 (4·0%) | 7/186 (1·9%) |
| Seizures within 24 hours before admission | 9/58 (14·8%) | 17/100 (16·5%) | 2/25 (8·0%) | 85/360 (23·3%) |
| Seizures outside 24 hours before admission | 3/56 (4·9%) | 2/95 (1·9%) | 1/24 (4·0%) | 13/340 (3·6%) |
| Neck stiffness | 8/46 (13·1%) | 3/73 (2·9%) | 2/20 (8·0%) | 13/265 (3·6%) |
| Neck pain | 4/38 (6·6%) | 3/57 (2·9%) | 1/15 (4·0%) | 3/207 (0·8%) |
| Altered consciousness\*\* | 24/56 (39·3%) | 30/96 (29·1%) | 10/24 (40·0%) | 85/343 (23·3%) |
| **SIGNS ON ADMISSION** |  |  |  |  |
| Temperature | 38·9 (38·3-39·5) [n=59] | 38·6 (38·0-39·1) [n=101] | 38·7 (38·0-39·3) [n=23] | 38·7 (38·0-39·2) [n=360] |
| Heart rate (/min) | 160·0 (145·5-182·2) [n=60] | 164·0 (150·0-183·0) [n=101] | 182·0 (168·5-188·5) [n=23] | 168·0 (149·8-182·0) [n=360] |
| Respiratory rate (/min) | 42·0 (32·0-52·8) [n=60] | 41·5 (35·0-48·0) [n=102] | 43·0 (40·0-48·0) [n=21] | 40·0 (34·2-48·0) [n=350] |
| Prolonged central capillary refill time | 7/33 (11·5%) | 5/47 (4·9%) | 1/9 (4·0%) | 35/202 (9·6%) |
| Respiratory signs | 26/60 (42·6%) | 21/100 (20·4%) | 8/22 (32·0%) | 92/356 (25·2%) |
| Photophobia | 2/25 (3·3%) | 0/36 (0·0%) | 0/11 (0·0%) | 4/164 (1·1%) |
| Neck stiffness | 10/35 (16·4%) | 2/40 (1·9%) | 2/11 (8·0%) | 8/170 (2·2%) |
| Kernig’s sign positive | 3/14 (4·9%) | 0/18 (0·0%) | 0/4 (0·0%) | 1/67 (0·3%) |
| Brudzinski’s sign positive | 0/13 (0·0%) | 0/18 (0·0%) | 0/4 (0·0%) | 0/62 (0·0%) |
| Rash |  |  |  |  |
| *Absent* | 39 (63·9%) | 49 (47·6%) | 4 (16·0%) | 240 (65·8%) |
| *Non-blanching* | 9 (14·8%) | 15 (14·6%) | 15 (60·0%) | 35 (9·6%) |
| *Other* | 6 (9·8%) | 26 (25·2%) | 4 (16·0%) | 62 (17·0%) |
| *Missing* | 7 (11·5%) | 13 (12·6%) | 2 (8·0%) | 28 (7·7%) |
| Fontanelle bulging (if open fontanelle) | 14/33 (23·0%) | 12/60 (11·7%) | 5/11 (20·0%) | 33/214 (9·0%) |
| GCS | 15·0 (13·0-15·0) [n=27] | 15·0 (15·0-15·0) [n=31] | 15·0 (11·0-15·0) [n=13] | 15·0 (15·0-15·0) [n=113] |

\* Including fast breathing, indrawing, grunting, apnoea, coryza, sore throat, cough, wheeze

\*\* Including drowsiness or coma

***Supplementary Table 7. Clinical signs and symptoms in children ≥12 months old with suspected meningitis***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Any bacterial meningitis | All aseptic meningitis | Possible meningitis | Control |
|  | N=58 | N=226 | N=42 | N=438 |
| Duration of symptoms prior to hospital presentation (median, IQR) | 2·0 (1·0-4·0) [n=53] | 4·0 (1·0-8·0) [n=219] | 1·0 (0·0-3·8) [n=42] | 2·0 (0·0-5·0) [n=415] |
| **SYMPTOMS** |  |  |  |  |
| Fever | 56/58 (96·6%) | 153/221 (67·7%) | 37/42 (88·1%) | 275/430 (62·8%) |
| Any respiratory symptoms\* | 33/57 (56·9%) | 75/217 (33·2%) | 19/40 (45·2%) | 192/426 (43·8%) |
| Rash | 24/55 (41·4%) | 36/215 (15·9%) | 19/42 (45·2%) | 90/418 (20·5%) |
| Vomiting | 54/57 (93·1%) | 134/224 (59·3%) | 31/41 (73·8%) | 204/422 (46·6%) |
| Diarrhoea | 8/57 (13·8%) | 35/219 (15·5%) | 9/40 (21·4%) | 70/417 (16·0%) |
| Headache | 23/37 (39·7%) | 122/199 (54·0%) | 20/36 (47·6%) | 119/323 (27·2%) |
| Seizures within 24 hours before admission | 9/57 (15·5%) | 60/222 (26·5%) | 9/42 (21·4%) | 195/424 (44·5%) |
| Seizures outside 24 hours before admission | 1/54 (1·7%) | 14/208 (6·2%) | 2/36 (4·8%) | 39/399 (8·9%) |
| Neck stiffness | 19/45 (32·8%) | 40/199 (17·7%) | 15/38 (35·7%) | 48/346 (11·0%) |
| Neck pain | 19/43 (32·8%) | 51/196 (22·6%) | 12/37 (28·6%) | 50/316 (11·4%) |
| Altered consciousness\*\* | 40/57 (69·0%) | 101/216 (44·7%) | 22/40 (52·4%) | 181/399 (41·3%) |
| **SIGNS ON ADMISSION** |  |  |  |  |
| Temperature | 38·8 (38·1-39·1) [n=56] | 38·0 (37·2-38·9) [n=206] | 38·4 (37·4-39·1) [n=41] | 38·3 (37·3-39·3) [n=405] |
| Heart rate (/min) | 130·0 (112·2-150·0) [n=56] | 110·0 (92·5-138·0) [n=211] | 126·0 (90·0-158·8) [n=42] | 132·0 (107·5-158·0) [n=415] |
| Respiratory rate (/min) | 32·0 (25·0-38·0) [n=56] | 25·0 (21·0-30·0) [n=205] | 28·0 (21·8-36·5) [n=40] | 28·0 (22·0-36·0) [n=396] |
| Prolonged central capillary refill time | 8/30 (13·8%) | 9/77 (4·0%) | 9/20 (21·4%) | 28/183 (6·4%) |
| Respiratory signs | 17/56 (29·3%) | 26/209 (11·5%) | 8/39 (19·0%) | 120/413 (27·4%) |
| Photophobia | 8/33 (13·8%) | 29/138 (12·8%) | 11/30 (26·2%) | 20/225 (4·6%) |
| Neck stiffness | 14/34 (24·1%) | 32/148 (14·2%) | 12/27 (28·6%) | 35/241 (8·0%) |
| Kernig’s sign positive | 2/17 (3·4%) | 8/77 (3·5%) | 4/15 (9·5%) | 7/110 (1·6%) |
| Brudzinski’s sign positive | 2/15 (3·4%) | 4/57 (1·8%) | 0/7 (0·0%) | 4/82 (0·9%) |
| Rash |  |  |  |  |
| *Absent* | 29 (50·0%) | 160 (70·8%) | 20 (47·6%) | 292 (66·7%) |
| *Non-blanching* | 19 (32·8%) | 15 (6·6%) | 18 (42·9%) | 53 (12·1%) |
| *Other* | 5 (8·6%) | 23 (10·2%) | 1 (2·4%) | 43 (9·8%) |
| *Missing* | 5 (8·6%) | 28 (12·4%) | 3 (7·1%) | 50 (11·4%) |
| Fontanelle bulging (if open fontanelle) | 1/4 (1·7%) | 0/6 (0·0%) | 0/3 (0·0%) | 1/20 (0·2%) |
| GCS | 13·0 (10·2-15·0) [n=42] | 15·0 (12·0-15·0) [n=148] | 14·0 (12·2-15·0) [n=22] | 14·0 (9·0-15·0) [n=260] |

\* Including fast breathing, indrawing, grunting, apnoea, coryza, sore throat, cough, wheeze

\*\* Including drowsiness or coma

***Supplementary Table 8. Laboratory parameters in children aged 0-28 days with suspected meningitis***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Any bacterial meningitis | All aseptic meningitis | Possible meningitis | Control |
|  | N=35 | N=177 | N=22 | N=454 |
| **BLOOD PARAMETERS (median, IQR)** |  |  |  |  |
| WBC count (X109/L) | 10·2 (5·4-19·2) [n=35] | 10·2 (7·2-13·5) [n=177] | 11·5 (6·3-13·3) [n=22] | 10·4 (7·9-13·8) [n=446] |
| Neutrophil count (X109/L) | 5·1 (2·5-13·0) [n=35] | 4·5 (3·1-7·0) [n=177] | 3·9 (2·7-6·5) [n=22] | 4·0 (2·6-6·9) [n=444] |
| Lymphocyte count (X109/L) | 2·4 (1·3-4·1) [n=34] | 3·8 (1·7-5·4) [n=177] | 3·7 (1·9-5·5) [n=22] | 3·9 (2·4-5·5) [n=442] |
| Blood CRP (mg/L) | 52·0 (8·7-117·6) [n=35] |  5·0 (2·5-14·8) [n=171] |  8·6 (2·5-30·4) [n=22] |  5·8 (2·5-23·0) [n=440] |
| **CSF PARAMETERS (median, IQR)** |  |  |  |  |
| Corrected CSF WBC count\* (X106/L) | 1022·5 (85·0-2829·0) [n=32] |  37·0 (1·8-366·5) [n=168] |  8·0 (2·0-16·0) [n=13] |  1·0 (0·5- 3·0) [n=391] |
| CSF neutrophil count (X106/L) | 612·0 (83·0-3018·0) [n=23] |  40·0 (6·0-225·0) [n=93] |  8·0 (5·0-15·8) [n=11] |  1·0 (0·0- 4·8) [n=81] |
| CSF lymphocyte count (X106/L) | 200·0 (48·5-537·5) [n=23] |  69·3 (10·0-221·0) [n=93] |  12·0 (7·0-15·0) [n=11] |  2·0 (1·0-7·0) [n=81] |
| CSF glucose (mmol/L) | 1·6 (0·8-2·6) [n=31] | 2·6 (2·3-2·9) [n=164] | 2·5 (2·1-2·8) [n=12] | 2·8 (2·5-3·2) [n=398] |
| CSF:plasma glucose ratio | 0·2 (0·2-0·5) [n=18] | 0·5 (0·5-0·7) [n=89] | 0·7 (0·7-0·8) [n=2] | 0·6 (0·5-0·7) [n=208] |
| CSF protein (g/L) | 2·1 (1·0-4·0) [n=28] | 0·7 (0·5-1·0) [n=153] | 1·0 (0·8-1·0) [n=11] | 0·7 (0·5-0·9) [n=381] |

\* Corrected by 500X106/L RBC:1 X106/L WBC

***Supplementary Table 9. Laboratory parameters in children aged between 29 days and <3 months with suspected meningitis***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Any bacterial meningitis | All aseptic meningitis | Possible meningitis | Control |
|  | N=49 | N=288 | N=15 | N=644 |
| **BLOOD PARAMETERS (median, IQR)** |  |  |  |  |
| WBC count (X109/L) |  9·6 (4·2-13·6) [n=48] | 10·1 (7·5-13·7) [n=282] | 10·2 (7·6-17·4) [n=15] | 10·4 (7·2-14·9) [n=627] |
| Neutrophil count (X109/L) | 3·8 (2·2-6·5) [n=48] | 3·7 (2·4-5·6) [n=281] | 3·9 (2·7-12·6) [n=15] | 3·9 (2·1-7·0) [n=624] |
| Lymphocyte count (X109/L) | 3·0 (1·6-6·0) [n=47] | 5·0 (2·7-7·0) [n=278] | 3·7 (2·5-4·6) [n=15] | 4·1 (2·5-6·1) [n=622] |
| Blood CRP (mg/L) | 52·0 (17·0-142·8) [n=47] |  5·0 (2·5-15·0) [n=283] | 13·0 (3·8-52·5) [n=15] | 12·0 (2·5-41·9) [n=630] |
| **CSF PARAMETERS (median, range)** |  |  |  |  |
| Corrected CSF WBC count\* (X106/L) | 104·0 (19·0-793·0) [n=45] |  23·0 (5·0-150·5) [n=270] |  0·5 (0·4-1·4) [n=8] |  0·5 (0·5-2·0) [n=557] |
| CSF neutrophil count (X106/L) | 86·8 (20·5-670·8) [n=30] | 19·4 (4·0-61·1) [n=142] |  2·2 (0·4-90·5) [n=4] |  0·5 (0·0-2·0) [n=81] |
| CSF lymphocyte count (X106/L) | 86·2 (11·4-207·8) [n=30] | 37·6 (10·0-159·1) [n=142] |  4·9 (0·0-44·9) [n=4] |  2·0 (0·5-4·0) [n=81] |
| CSF glucose (mmol/L) | 2·7 (1·4-3·2) [n=44] | 2·8 (2·5-3·1) [n=271] | 3·2 (2·8-3·8) [n=10] | 3·0 (2·7-3·3) [n=575] |
| CSF:plasma glucose ratio | 0·5 (0·4-0·6) [n=23] | 0·5 (0·5-0·6) [n=137] | 0·6 (0·6-0·6) [n=5] | 0·6 (0·5-0·6) [n=267] |
| CSF protein (g/L) | 0·7 (0·5-2·5) [n=40] | 0·5 (0·4-0·8) [n=258] | 0·6 (0·4-0·8) [n=8] | 0·4 (0·3-0·6) [n=558] |

\* Corrected by 500X106/L RBC:1 X106/L WBC

***Supplementary Table 10. Laboratory parameters in children aged between 3 months and 11 months with suspected meningitis***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Any bacterial meningitis | All aseptic meningitis | Possible meningitis | Control |
|  | N=61 | N=103 | N=25 | N=365 |
| **BLOOD PARAMETERS (median, IQR)** |  |  |  |  |
| WBC count (X109/L) | 15·9 (9·0-22·2) [n=60] | 12·9 (9·4-18·6) [n=102] | 10·8 (7·4-20·5) [n=25] | 14·1 (9·6-19·8) [n=358] |
| Neutrophil count (X109/L) | 10·7 (5·2-15·8) [n=60] |  6·1 (4·1-11·0) [n=102] |  6·0 (3·1-10·0) [n=24] |  7·1 (4·0-11·4) [n=355] |
| Lymphocyte count (X109/L) | 2·8 (2·1-5·4) [n=59] | 4·7 (3·2-6·1) [n=102] | 3·3 (2·7-5·3) [n=23] | 4·8 (2·8-6·8) [n=354] |
| Blood CRP (mg/L) | 163·0 (110·0-230·0) [n=61] |  18·2 ( 4·0-72·8) [n=101] |  56·6 (28·0-104·8) [n=24] |  24·4 ( 6·3-65·1) [n=357] |
| **CSF PARAMETERS (median, range)** |  |  |  |  |
| Corrected CSF WBC count\* (X106/L) | 231·0 (65·0-816·0) [n=57] |  22·5 (6·0-121·0) [n=102] |  2·0 (0·5-4·0) [n=13] |  0·5 (0·5-2·0) [n=333] |
| CSF neutrophil count (X106/L) | 170·0 (39·9-493·8) [n=47] |  17·1 (5·2-71·0) [n=55] |  2·0 (1·1-3·0) [n=5] |  0·5 (0·0-2·0) [n=31] |
| CSF lymphocyte count (X106/L) | 90·0 (21·1-263·8) [n=47] | 30·0 (11·7-67·0) [n=55] |  3·0 (1·2-13·8) [n=6] |  1·0 (0·0-2·5) [n=31] |
| CSF glucose (mmol/L) | 2·1 (0·8-3·2) [n=50] | 3·2 (2·9-3·6) [n=96] | 2·9 (2·7-3·6) [n=14] | 3·4 (3·2-3·8) [n=336] |
| CSF:plasma glucose ratio | 0·4 (0·1-0·6) [n=31] | 0·6 (0·5-0·6) [n=47] | 0·6 (0·5-0·6) [n=9] | 0·6 (0·6-0·7) [n=162] |
| CSF protein (g/L) | 1·0 (0·4-2·0) [n=54] | 0·3 (0·2-0·6) [n=94] | 0·2 (0·2-0·5) [n=15] | 0·2 (0·1-0·3) [n=322] |

\* Corrected by 500X106/L RBC:1 X106/L WBC

***Supplementary Table 11. Laboratory parameters in children ≥12 months old with suspected meningitis***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Any bacterial meningitis | All aseptic meningitis | Possible meningitis | Control |
|  | N=58 | N=226 | N=42 | N=438 |
| **BLOOD PARAMETERS (median, IQR)** |  |  |  |  |
| WBC count (X109/L) | 16·2 (10·5-24·1) [n=57] | 11·5 (8·4-16·7) [n=223] | 12·7 (9·1-18·6) [n=42] | 11·3 (7·8-16·6) [n=423] |
| Neutrophil count (X109/L) | 13·3 (7·3-19·3) [n=57] |  7·4 (4·8-11·8) [n=222] |  9·9 (4·6-14·9) [n=42] |  7·3 (3·9-11·4) [n=422] |
| Lymphocyte count (X109/L) | 1·3 (1·0-2·4) [n=54] | 2·0 (1·2-3·4) [n=214] | 1·4 (0·9-2·7) [n=42] | 2·5 (1·5-4·1) [n=417] |
| Blood CRP (mg/L) | 184·0 (82·0-256·0) [n=57] |  7·6 (2·5-39·0) [n=221] |  41·1 (8·8-127·0) [n=42] |  9·3 (2·5-47·1) [n=408] |
| **CSF PARAMETERS (median, range)** |  |  |  |  |
| Corrected CSF WBC count\* (X106/L) | 505·0 (122·0-1505·0) [n=55] |  18·0 ( 3·0-68·0) [n=212] |  0·5 ( 0·5- 0·9) [n=14] |  0·5 ( 0·5- 2·0) [n=376] |
| CSF neutrophil count (X106/L) | 168·6 (43·9-896·2) [n=44] |  6·0 ( 1·0-34·1) [n=112] | 224·7 (224·7-224·7) [n=1] |  0·0 ( 0·0-1·0) [n=31] |
| CSF lymphocyte count (X106/L) | 203·4 (43·1-484·2) [n=44] |  36·0 (11·4-99·6) [n=113] |  96·3 (96·3-96·3) [n=1] |  1·0 (0·0-2·0) [n=31] |
| CSF glucose (mmol/L) | 2·5 (1·1-3·4) [n=49] | 3·3 (2·9-3·8) [n=206] | 3·4 (3·2-3·8) [n=19] | 3·5 (3·1-3·9) [n=365] |
| CSF:plasma glucose ratio | 0·5 (0·2-0·6) [n=18] | 0·6 (0·5-0·7) [n=80] | 0·7 (0·6-0·7) [n=10] | 0·7 (0·6-0·8) [n=157] |
| CSF protein (g/L) | 0·9 (0·5-1·8) [n=48] | 0·3 (0·2-0·5) [n=203] | 0·3 (0·2-0·4) [n=17] | 0·2 (0·1-0·2) [n=366] |

\* Corrected by 500X106/L RBC:1 X106/L WBC

***Supplementary Table 12: Pre- and Post-LP points score system***

|  |  |  |
| --- | --- | --- |
| Variables | Coefficient | Score |
| **Pre-LP**  |
| Vomiting | 0·6 | 0·5 |
| Altered consciousness | 0·2 | 0·5 |
| Bulging fontanelle | 2·1 | 2 |
| Lymphocyte count <2·4 x109/L\* | 1·3 | 1·5 |
| CRP >50·9 mg/L\* | 2·4 | 2·5 |
| **Post-LP** |
| Rash |  |  |
| Non-blanching | 1·6 | 1·5 |
| Other | Ref | 0 |
| No rash | 0·6 | 0·5 |
| Lymphocyte count <2·9 x109/L\* | 0·9 | 1 |
| CRP >50·5 mg/L\* | 2·6 | 2·5 |
| CSF glucose <2·15 mmol/L\* | 1·4 | 1·5 |
| CSF protein >1·15 g/L\* | 1·0 | 1·0 |
| CSF WBC > 187·5 x106/L \* | 1·1 | 1·0 |
| CSF neutrophils > 66·25 x106/L \* | 1·1 | 1·0 |

\* cut-off was determined by ROC to maximise the accuracy in distinguishing participants with and without bacterial meningitis.

***Supplementary Table 13: UK-ChiMES and ENCEPH-UK study groups member list not included as named authors (listed alphabetically)***

|  |  |
| --- | --- |
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