# Treatment Outcomes of Childhood Tuberculous Meningitis in a Real-World Retrospective Cohort, Bandung, Indonesia

**Appendix**

## Assessments of neurologic sequelae in children with tuberculous meningitis at treatment completion

In this study, neurologic sequelae were defined as any motor, hearing, visual or neurodevelopmental impairment that appeared during the illness and persisted through treatment completion. Only severe neurologic sequelae were recorded in the database. Mild to moderate sequelae were not routinely tested or recorded, and complete assessments were only performed if indicated or requested by the attending physicians. Generally, hearing function was assessed using the Brainstem Auditory Evoked Response (BAER) method. Degree of hearing loss was determined based on the Pure Tone Average (PTA). Visual examinations consisted of a visual acuity test using Cardiff Acuity Cards or the Snellen Chart, an extraocular muscle examination test, the anterior segment of the eyeball examination test using a slit lamp or a loop/magnifier 3D and a penlight, and the posterior segment of the eyeball/fundus examination test using direct and indirect ophthalmoscope. Neurodevelopmental function in children aged ≤8 years was assessed using the Griffiths General Developmental Quotient. In children aged >8 years, neurodevelopmental function was assessed using the Wechsler Intelligence Scale for Children (WISC). Gross motor function was assessed using the Growth Motor Functional Measurement (GMFM). Detailed methods and classifications have been described elsewhere (1).

## Case presentation of a TBM patient with SARS-CoV-2 coinfection

A 6-month-old boy (weight: 5.3 kg, height: 60 cm, head circumference: 46 cm) presented at Hasan Sadikin Hospital in April 2020, with a 10-day history of fever prior to admission. He also had seizures, quadriparesis and vomiting, but no other symptoms suggestive of TBM were

reported at presentation. Prior to admission, he had a diagnosis of congenital hydrocephalus and underwent a ventriculoperitoneal shunt in another hospital. He had an unknown history of recent close contact with a TB patient, had been vaccinated with BCG, was severely malnourished and had a GCS score of 15 with focal neurologic deficits. In cerebrospinal fluid (CSF) analysis, he had pleocytosis of 355 cells/μL, abnormal protein concentration of 848 mg/dL, lymphocytic predominance of 59.7%, CSF to blood glucose ratio of 30% and smear-negative for acid fast-bacilli (AFB). He had a negative result on tuberculin skin test and had bronchopneumonia dextra on chest radiography. Mycobacterial cultures from CSF and gastric lavage were negative, AFB smear microscopy was positive from gastric lavage, and *M. tuberculosis* sensitive to rifampicin was identified through GeneXpert MTB/RIF assay from gastric lavage. Brain computed tomography scan results showed communicating hydrocephalus, with negative signs for basal meningeal enhancement, infarct or tuberculoma. He was diagnosed with probable TBM at stage II, and was treated with daily oral isoniazid at 10 mg/kg, rifampicin at 15 mg/kg, pyrazinamide at 35 mg/kg and ethambutol at 20 mg/kg, for a 2-month intensive phase, and followed by a 10-month continuation therapy with isoniazid and rifampicin at the same doses. Adjunctive oral prednisone at 2 mg/kg was given for the first 4 weeks of treatment. During hospitalization, facility-based directly observed treatment was used by the treated physician or nurses to administer the drugs. He was discharged after 20 days of hospitalization, with existing complications of hearing impairment and motor disorders.

After discharge, TBM treatment with first-line anti-TB drugs was continued for up to 12 months, and he was followed up monthly at Hasan Sadikin Hospital. During the 8-month follow-up, he was tested positive for coronavirus SARS-CoV-2 infection by real-time reverse transcription-polymerase chain reaction swab test (RdRp- and E-genes), with no specific symptoms for COVID-19. After 1 day of hospitalization, he was discharged and advised to self-isolate for 3 weeks. No antiretroviral drugs were administered. After 3 weeks, he was confirmed negative from SARS-CoV-2. At treatment completion, TBM symptoms of fever and seizures were not present. Bodyweight, height and head circumference had increased to 9.8 kg, 81 cm and 52 cm, respectively. Neurologic sequelae of motor disorders persisted through treatment completion. He was considered a failure to thrive, with only being able to tilt his body to the right and unable to babble.

**Appendix Table 1.** Diagnostic certainty of tuberculous meningitis using uniform case definition criteria by Marais et al (2).

| Characteristic | Score | Total patients (n=283) | Possible/ probable TBM (n=232) |
|---|---|---|---|
| Clinical criteria [maximum category score = 6] | | | |
| Symptoms duration of more than 5 days | 4 | 234 (82.7) | 191 (82.3) |
| Systemic symptoms suggestive of TB (one or more of the following: weight loss / poor weight gain, night sweats, or persistent cough for more than 2 weeks) | 2 | 263 (92.9) | 216 (93.1) |
| History of recent (within past year) close contact with an individual with pulmonary TB or a positive TST or IGRA (only in children under 10 years of age) | 2 | 114 (40.3) | 94 (40.5) |
| Focal neurologic deficit (excluding cranial nerve palsies) | 1 | 222 (78.4) | 179 (77.2) |
| Cranial nerve palsy | 1 | 48 (17.0) | 36 (15.5) |
| Altered consciousness | 1 | 211 (74.6) | 169 (72.8) |
| CSF criteria [maximum category score = 4) | | | |
| Clear appearance | 1 | 276 (97.5) | 225 (97.0) |
| Leucocyte cells: 10-500 per µL | 1 | 212 (74.9) | 172 (74.1) |
| Lymphocytic predominance of >50% | 1 | 225 (79.5) | 182 (78.4) |
| Protein concentration >100 mg/dL | 1 | 143 (50.5) | 115 (49.6) |
| CSF / plasma glucose ratio of <50% or an absolute CSF glucose concentration <40 mg/dL | 1 | 142 (50.0) | 115 (49.6) |
| Cerebral imaging criteria [maximum category score = 6] | | | |
| Hydrocephalus | 1 | 103 (41.2) | 84 (36.2) |
| Basal meningeal enhancement | 2 | 131 (46.3) | 104 (44.8) |
| Tuberculoma | 2 | 31 (11.0) | 22 (9.5) |
| Infarct | 1 | 25 (8.8) | 21 (9.1) |
| Pre-contrast basal hyperdensity | 2 | - | - |
| Evidence of TB elsewhere [maximum category score = 4] | | | |
| Chest radiography suggestive of active TB | | | |
| Miliary TB | 4 | 19 (6.7) | 16 (6.9) |
| Other signs of TB | 2 | 128 (45.2) | 103 (44.4) |
| CT / MRI / USG evidence of TB outside the CNS | 2 | - | - |
| AFB identified or *M. tuberculosis* cultured from another source (sputum, lymph node, gastric aspirates, urine or blood culture) | 4 | 65 (23.0) | 37 (15.9) |
| Positive commercial *M. tuberculosis* nucleic acid amplification test (NAAT) from non-CSF specimen | 4 | 76 (26.8) | 38 (16.4) |
| Definite TBM (AFB seen on CSF microscopy, *M. tb* cultured from CSF, or *M. tb* detected through GeneXpert test) | | 51 (18.0) | |
| Probable TBM (total score of ≥12 when neuroimaging available or total score of ≥10 when neuroimaging was unavailable) | | 178 (62.9) | |
| Possible TBM (total score of 6-11 when neuroimaging available, or total score of 6-9 when neuroimaging was unavailable) | | 54 (19.1) | |

**Appendix Table 2.** Operational definition for variables used in this study

| Variable | Definition |
|---|---|
| Children | Individuals aged <15 years at diagnosis were defined as children, and were generally categorized by three age bands (0-4 years, 5-9 years and 10-14 years) as recommended by the WHO (3). An age group of less than 2 years was added given the high risk of severe progression to miliary and meningitis TB following infection with *M. tuberculosis* (4). |
| Malnourished | Children aged <5 years with weight-for-age or height-for-age Z-scores <-2 standard deviations, or children aged ≥5 years with height-for-age or BMI-for-age Z-scores <-2 standard deviation (5,6). |
| Known TB contact history | A patient who had close contact history with an infectious TB patient within the past year before hospital admission. |
| Known BCG vaccination | A documented BCG vaccination history in the immunization records book (*Buku Kesehatan Ibu dan Anak)* at the time of hospital admission, and/or the presence of a BCG scar in the deltoid part of the upper arm. |
| Definite TBM | Microbiological confirmation from CSF examination, including AFB smear microscopy, mycobacterial culture or GeneXpert MTB/RIF testing (2). |
| Probable TBM | A total diagnostic score of ≥12 when neuroimaging was available, or ≥10 when neuroimaging was unavailable (2). |
| Possible TBM | A total diagnostic score of 6-11 when neuroimaging was available, or 6-9 when neuroimaging was unavailable (2). |
| TBM stage I | Glasgow Coma Scale (GCS) scores of 15 without focal neurologic signs (7). |
| TBM stage II | GCS scores of 11-14 or 15 with focal neurologic signs (7). |
| TBM stage III | GCS scores of ≤10 (7). |

| Variable | Definition |
|---|---|
| Cranial nerve palsy | Cranial nerve palsy was characterized by a decreased or complete loss function of one or more cranial nerves. |
| Motor deficits | Motor deficits included hemiparesis, quadriparesis and diplegia. |
| Signs of upper neuron lesion | Signs of upper motor neuron lesion included muscle weakness, hypertonus, clonus, hyperreflexia and the presence of pathological reflex. |
| Signs raised intracranial pressure | In physical examination, signs of raised intracranial pressure could include cranial nerve IV palsy, excessive headache/vomiting, papilledema, bulging fontanelle, sunsetting sign, etc. The diagnosis could also be made through cerebral imaging. |
| Hydrocephalus on neuroimaging | Enlargement of the ventricles with the compression of sulci and gyri and enlargement of temporal horn >2 mm or frontal horn-to-internal diameter ratio >0.5, supported by ballooning of the frontal horns, transependymal edema, Evans ratio of >0.3, and sagittal bowing of corpus callosum (8). |
| Suggestive of TB from chest radiography | Chest radiographic findings suggestive of TB included mediastinal/hilar lymphadenopathy, segmental infiltration and/or collapse, pleural effusion, cavitation, and signs of miliary TB. |
| Positive tuberculin skin test | Induration of ≥10 mm in Mantoux skin test, or ≥5 mm in patients with severe malnutrition or HIV-infected children. |
| AFB smear positive | The specimen from cerebrospinal fluid, sputum, gastric lavage or other body materials noted as at least +1 for acid-fast bacilli (AFB) on microscopy using Ziehl-Neelsen stain. |
| Anti-TB drug-induced hepatotoxicity | Anti-TB drug-induced hepatotoxicity was defined according to the modified American Thoracic Society guidelines, developed internally by the Department of Child Health, Universitas Padjadjaran, as follows: an elevation of alanine aminotransferase (ALT) >3× the ULN with symptoms of hepatotoxicity, an elevation of ALT >5× the ULN without symptoms, normal baseline ALT with the presence of jaundice, anorexia, nausea and vomiting during treatment, or an increased in total bilirubin level >1.5 mg/dL (9,10). |

**Appendix Table 3.** Symptoms of tuberculous meningitis at presentation stratified by disease staging, in children with tuberculous meningitis treated at Hasan Sadikin Hospital, Bandung, Indonesia, 2011–2020

| Symptom | Stage I N* | Stage I Value | Stage II N* | Stage II Value | Stage III N* | Stage III Value |
|---|---|---|---|---|---|---|
| Fever | 57 | 46 (80.7) | 131 | 122 (93.1) | 95 | 82 (86.3) |
| Severe headache | 56 | 15 (26.8) | 131 | 31 (23.7) | 91 | 15 (15.8) |
| Muscle weakness | 57 | 12 (21.1) | 129 | 36 (27.5) | 92 | 25 (26.3) |
| Altered consciousness | 57 | 18 (31.6) | 131 | 110 (84.0) | 95 | 83 (87.4) |
| Seizures | 57 | 28 (49.1) | 131 | 63 (48.1) | 95 | 64 (67.4) |
| Shortness of breath | 57 | 13 (22.8) | 130 | 14 (10.7) | 93 | 17 (17.9) |
| Persistent cough | 57 | 21 (36.8) | 131 | 41 (31.3) | 94 | 33 (35.1) |
| Poor weight gain / weight loss | 57 | 16 (28.1) | 130 | 44 (33.6) | 92 | 45 (47.4) |

Data are presented as number (n) with percentages (%). *: Number of total patients for which data were available. Stage I TBM was defined as Glasgow Coma Scale (GCS) of 15 with no focal neurologic signs, stage II TBM as GCS of 11-14 or 15 with focal neurologic signs, and stage III TBM as GCS ≤10 (7).

**Appendix Table 4.** Univariate Cox proportional-hazards regression model for factors associated with in-hospital death in children treated for tuberculous meningitis at Hasan Sadikin Hospital, Bandung, Indonesia, 2011–2020

| Patient characteristics | Dead (n=44) | Alive (n=231) | cHR (95% CI) | p-value |
|---|---|---|---|---|
| Year of diagnosis (median (IQR))[a,b] | 2018 (2015-2019) | 2016 (2014-2019) | 1.11 (0.98-1.25) | 0.087 |
| Year of diagnosis[a,b] | | | | |
| 2011-2015 | 11 (25.0) | 91 (39.4) | 0.55 (0.28-1.08) | 0.083 |
| 2016-2020 | 33 (75.0) | 140 (60.6) | 1.00 | |
| Age, years (median (IQR)) | 4.0 (1.5-10.7) | 1.0 (4.0-10.0) | 1.00 (0.94-1.07) | 0.876 |
| Age[a] | | | | |
| <2 years | 13 (29.5) | 78 (33.8) | 0.78 (0.37-1.67) | 0.527 |
| 2-4 years | 11 (25.0) | 47 (20.3) | 1.04 (0.47-2.29) | 0.992 |
| 5-9 years | 6 (13.6) | 43 (18.6) | 0.65 (0.25-1.70) | 0.384 |
| 10-14 years | 14 (31.8) | 63 (27.3) | 1.00 | |
| Sex[a] | | | | |
| Male | 29 (65.9) | 118 (51.1) | 1.72 (0.92-3.20) | 0.089 |
| Female | 15 (34.1) | 113 (48.9) | 1.00 | |
| Parent's last education | | | | |
| Elementary | 4 (9.1) | 38 (16.5) | 0.83 (0.15-4.53) | 0.829 |
| Junior high school | 16 (36.4) | 64 (27.7) | 1.88 (0.43-8.16) | 0.401 |
| Senior high school | 21 (47.7) | 110 (47.6) | 1.47 (0.34-6.25) | 0.605 |
| University | 2 (4.5) | 15 (6.5) | 1.00 | |
| Parent's monthly income[a] | | | | |
| USD ≤140,00 | 33 (75.0) | 136 (58.9) | 2.79 (1.17-6.67) | 0.021 |
| USD >140,00 | 6 (13.6) | 74 (32.0) | 1.00 | |
| Area of living | | | | |
| Urban | 17 (38.6) | 98 (42.4) | 1.00 | |

| Patient characteristics | Dead (n=44) | Alive (n=231) | cHR (95% CI) | p-value |
|---|---|---|---|---|
| Rural | 25 (56.8) | 126 (54.5) | 1.13 (0.61-2.10) | 0.692 |
| Weight-for-age Z-score | | | | |
| ≥-2 (normal) | 19 (43.2) | 82 (35.5) | 1.00 | |
| <-2 (underweight) | 17 (38.6) | 103 (44.6) | 0.72 (0.38-1.39) | 0.336 |
| Height-for-age Z-score | | | | |
| ≥-2 (normal) | 24 (54.5) | 141 (61.0) | 1.00 | |
| <-2 (stunted) | 20 (45.5) | 90 (39.0) | 1.25 (0.69-2.26) | 0.460 |
| Weight-for-height Z-score | | | | |
| ≥-2 (normal) | 21 (47.7) | 115 (49.8) | 1.00 | |
| <-2 (wasted) | 23 (52.3) | 116 (50.2) | 1.06 (0.59-1.92) | 0.837 |
| BMI-for-age Z-score | | | | |
| ≥-2 (normal) | 22 (50.0) | 113 (48.9) | 1.00 | |
| <-2 (low BMI) | 22 (50.0) | 118 (51.1) | 0.96 (0.53-1.72) | 0.881 |
| Nutritional status[§] | | | | |
| Normal | 16 (36.4) | 81 (35.1) | 1.00 | |
| Moderate malnutrition | 10 (22.7) | 60 (26.0) | 0.82 (0.37-1.82) | 0.634 |
| Severe malnutrition | 18 (40.9) | 90 (39.0) | 1.00 (0.51-1.95) | 0.991 |
| Known BCG vaccination[a] | | | | |
| No | 15 (34.1) | 44 (19.0) | 2.01 (1.08-3.76) | 0.028 |
| Yes | 29 (65.9) | 187 (81.0) | 1.00 | |
| Known TB contact history[a] | | | | |
| No | 27 (61.4) | 176 (76.2) | 1.00 | |
| Yes | 17 (38.6) | 55 (23.8) | 1.83 (1.00-3.35) | 0.051 |
| Known HIV status[a,e] | | | | |
| No/unknown | 41 (93.2) | 230 (99.6) | 1.00 | |
| Yes | 3 (6.8) | 1 (0.4) | 6.46 (1.99-20.92) | 0.002 |
| *TBM category and stage* | | | | |
| TBM category[¥] | | | | |
| Definite TBM | 9 (20.5) | 39 (16.9) | 1.00 | |
| Probable TBM | 25 (56.8) | 147 (63.6) | 0.72 (0.34-1.55) | 0.406 |
| Possible TBM | 10 (22.7) | 45 (19.5) | 0.93 (0.38-2.29) | 0.857 |
| TBM stage[¶,a,c] | | | | |
| Stage I | 2 (4.5) | 54 (23.4) | 1.00 | |
| Stage II | 15 (34.1) | 111 (48.1) | 3.53 (0.81-15.44) | 0.094 |
| Stage III | 27 (61.4) | 66 (28.6) | 9.16 (2.18-38.51) | 0.003 |
| GCS (median (IQR))[a,c] | 10 (9-12) | 12 (11-15) | 0.80 (0.72-0.88) | <0.001 |
| *Presenting symptoms* | | | | |
| Fever | | | | |
| No | 6 (13.6) | 27 (11.7) | 1.00 | |
| Yes | 38 (86.4) | 204 (88.3) | 0.87 (0.37-2.07) | 0.759 |
| Severe headache | | | | |
| No | 31 (70.5) | 179 (77.5) | 1.00 | |
| Yes | 11 (25.0) | 49 (21.2) | 1.30 (0.66-2.60) | 0.448 |
| Muscle weakness | | | | |
| No | 33 (75.0) | 169 (73.2) | 1.00 | |
| Yes | 10 (22.7) | 58 (25.1) | 0.87 (0.43-1.76) | 0.700 |
| Altered consciousness | | | | |
| No | 7 (15.9) | 64 (27.7) | 1.00 | |
| Yes | 37 (84.1) | 167 (72.3) | 1.91 (0.85-4.30) | 0.115 |
| Seizures[a] | | | | |
| No | 13 (29.5) | 112 (49.5) | 1.00 | |
| Yes | 31 (70.5) | 119 (51.5) | 2.09 (1.09-3.99) | 0.026 |
| Shortness of breath[a] | | | | |
| No | 32 (72.7) | 196 (84.8) | 1.00 | |
| Yes | 11 (25.0) | 33 (14.3) | 1.81 (0.91-3.59) | 0.090 |
| Persistent cough | | | | |
| No | 27 (61.4) | 155 (67.1) | 1.00 | |
| Yes | 16 (36.4) | 76 (32.9) | 1.20 (0.64-2.22) | 0.567 |
| Poor weight gain / weight loss | | | | |
| No | 26 (59.1) | 142 (61.5) | 1.00 | |
| Yes | 17 (38.6) | 86 (37.2) | 1.06 (0.57-1.95) | 0.861 |
| Duration of symptoms | | | | |
| 0-7 days | 15 (34.1) | 84 (36.4) | 1.00 | |
| 8-14 days | 25 (56.8) | 119 (51.5) | 1.16 (0.61-2.19) | 0.658 |
| >14 days | 1 (2.3) | 17 (7.4) | 0.34 (0.04-2.58) | 0.298 |
| *Examination findings at baseline* | | | | |
| Body temperature | | | | |
| <38 °C | 33 (75.0) | 181 (78.4) | 1.00 | |
| ≥38 °C | 10 (22.7) | 50 (21.6) | 1.06 (0.52-2.16) | 0.865 |

| Patient characteristics | Dead (n=44) | Alive (n=231) | cHR (95% CI) | p-value |
|---|---|---|---|---|
| Respiration rate | | | | |
|   <25/min | 11 (25.0) | 78 (33.8) | 1.00 | |
|   ≥25/min | 32 (72.7) | 151 (65.4) | 1.43 (0.72-2.84) | 0.304 |
| Involuntary movement | | | | |
|   No | 36 (81.8) | 203 (87.9) | 1.00 | |
|   Yes | 6 (13.6) | 22 (9.5) | 1.54 (0.65-3.65) | 0.329 |
| Cranial nerve palsies | | | | |
|   No | 34 (77.3) | 187 (81.0) | 1.00 | |
|   Yes | 8 (18.2) | 40 (17.3) | 1.14 (0.53-2.47) | 0.736 |
| Any type of motor deficit | | | | |
|   No | 20 (45.5) | 90 (39.0) | 1.00 | |
|   Yes | 21 (47.7) | 124 (53.7) | 0.82 (0.44-1.50) | 0.515 |
| Unequal pupils | | | | |
|   No | 39 (88.6) | 221 (95.7) | 1.00 | |
|   Yes | 3 (6.8) | 6 (2.6) | 2.49 (0.77-8.07) | 0.127 |
| Signs of upper motor neuron lesions[a] | | | | |
|   No | 6 (13.6) | 64 (27.7) | 1.00 | |
|   Yes | 36 (81.8) | 150 (64.9) | 2.46 (1.03-5.83) | 0.042 |
| Signs of raised intracranial pressure[a,d] | | | | |
|   No | 25 (56.8) | 203 (87.9) | 1.00 | |
|   Yes | 19 (43.2) | 28 (12.1) | 4.39 (2.41-7.97) | <0.001 |
| *CSF findings* | | | | |
| Leucocyte ≥10 cells/µL[a] | | | | |
|   No | 14 (31.8) | 48 (20.8) | 1.00 | |
|   Yes | 27 (61.4) | 179 (77.5) | 0.56 (0.29-1.06) | 0.076 |
| Leucocyte ≥100 cells/µL | | | | |
|   No | 32 (72.7) | 160 (69.3) | 1.00 | |
|   Yes | 9 (20.5) | 67 (29.0) | 0.71 (0.34-1.49) | 0.370 |
| Lymphocytic predominance >50% | | | | |
|   No | 8 (18.2) | 40 (17.3) | 1.00 | |
|   Yes | 34 (77.3) | 185 (80.1) | 0.93 (0.43-2.00) | 0.846 |
| Protein >100 mg/dL | | | | |
|   No | 22 (50.0) | 107 (46.3) | 1.00 | |
|   Yes | 20 (45.5) | 119 (51.5) | 0.82 (0.45-1.51) | 0.532 |
| Glucose <40 mg/dL | | | | |
|   No | 22 (50.0) | 133 (57.6) | 1.00 | |
|   Yes | 20 (45.5) | 86 (37.2) | 1.36 (0.74-2.49) | 0.322 |
| CSF/blood glucose ratio <50% | | | | |
|   No | 15 (34.1) | 93 (40.3) | 1.00 | |
|   Yes | 22 (50.0) | 103 (44.6) | 1.31 (0.68-2.53) | 0.417 |
| *Radiological findings* | | | | |
| Chest radiography | | | | |
|   Normal | 23 (52.3) | 108 (46.8) | 1.00 | |
|   Miliary TB | 2 (4.5) | 17 (7.4) | 0.57 (0.13-2.42) | 0.448 |
|   Other signs of TB | 19 (43.2) | 104 (45.0) | 0.88 (0.48-1.62) | 0.682 |
| Hydrocephalus[a,d] | | | | |
|   No | 12 (27.3) | 133 (57.6) | 1.00 | |
|   Yes | 22 (50.0) | 76 (32.9) | 3.00 (1.48-6.05) | 0.002 |
|     Neurosurgery in hydrocephalus patients[§§] | | | | |
|       No | 13 (59.1) | 40 (52.6) | 1.25 (0.53-2.93) | 0.604 |
|       Yes | 9 (40.9) | 36 (47.4) | 1.00 | |
| Basal meningeal enhancement | | | | |
|   No | 14 (31.8) | 101 (43.7) | 1.00 | |
|   Yes | 20 (45.5) | 108 (46.8) | 1.30 (0.66-2.58) | 0.445 |
| Cerebral infarct | | | | |
|   No | 30 (68.2) | 189 (81.8) | 1.00 | |
|   Yes | 4 (9.1) | 20 (8.7) | 1.23 (0.43-3.51) | 0.692 |
| Tuberculoma | | | | |
|   No | 28 (63.6) | 185 (80.1) | 1.00 | |
|   Yes | 6 (13.6) | 24 (10.4) | 1.59 (0.66-3.84) | 0.302 |
| At least 1 sign found on CT scan | | | | |
|   No | 7 (15.9) | 67 (29.0) | 1.00 | |
|   Yes | 27 (61.4) | 142 (61.5) | 1.76 (0.77-4.04) | 0.183 |
| *Bacteriological findings* | | | | |
| TST positive | | | | |
|   No | 38 (86.4) | 176 (76.2) | 1.00 | |
|   Yes | 6 (13.6) | 55 (23.8) | 0.54 (0.23-1.28) | 0.164 |
| GeneXpert MTB/RIF testing | | | | |
|   Negative | 25 (56.8) | 135 (58.4) | 1.00 | |

| Patient characteristics | Dead (n=44) | Alive (n=231) | cHR (95% CI) | p-value |
|---|---|---|---|---|
| *M.tb* identified from CSF | 8 (18.2) | 37 (16.0) | 1.21 (0.55-2.69) | 0.632 |
| *M.tb* identified from non-CSF | 5 (11.4) | 34 (14.7) | 0.81 (0.31-2.13) | 0.675 |
| AFB smear microscopy | | | | |
| Negative | 33 (75.0) | 184 (79.7) | 1.00 | |
| Positive from CSF | 2 (4.5) | 4 (1.7) | 2.44 (0.59-10.19) | 0.220 |
| Positive from non-CSF | 7 (15.9) | 34 (14.7) | 1.15 (0.51-2.60) | 0.737 |
| *M. tb* cultured from any source | | | | |
| No | 36 (81.8) | 200 (86.6) | 1.00 | |
| Yes | 2 (4.5) | 21 (9.1) | 0.56 (0.13-2.34) | 0.429 |
| *In-hospital complications* | | | | |
| Motor disorders | | | | |
| No | 31 (70.5) | 142 (61.5) | 1.00 | |
| Yes | 12 (27.3) | 89 (38.5) | 0.66 (0.34-1.28) | 0.216 |
| Visual impairment | | | | |
| No | 42 (95.5) | 215 (93.1) | 1.00 | |
| Yes | 1 (2.3) | 16 (6.9) | 0.33 (0.05-2.40) | 0.275 |
| Hearing impairment | | | | |
| No | 41 (93.2) | 221 (95.7) | 1.00 | |
| Yes | 2 (4.5) | 10 (4.3) | 1.13 (0.27-4.69) | 0.862 |
| Neurodevelopmental delay | | | | |
| No | 37 (84.1) | 200 (86.6) | 1.00 | |
| Yes | 6 (13.6) | 31 (13.4) | 1.05 (0.44-2.49) | 0.913 |
| Epileptic seizures | | | | |
| No | 39 (88.6) | 217 (93.9) | 1.00 | |
| Yes | 5 (11.4) | 14 (6.1) | 1.81 (0.71-4.59) | 0.212 |
| Anti-TB drug-induced hepatotoxicity | | | | |
| No | 39 (88.6) | 209 (90.5) | 1.00 | |
| Yes | 5 (11.4) | 22 (9.5) | 1.21 (0.47-3.06) | 0.693 |
| *Others* | | | | |
| Oral corticosteroid | | | | |
| No | 2 (4.5) | 10 (4.3) | 1.00 | |
| Yes | 40 (90.9) | 214 (92.6) | 0.94 (0.23-3.88) | 0.931 |

cHR: crude hazard ratio, AFB: acid-fast bacilli, BCG: Bacillus Calmette-Guerin, CSF: cerebrospinal fluid, CI: confidence interval, GCS: Glasgow Coma Scale, HIV: human immunodeficiency virus, IQR: interquartile rage, TB: tuberculosis, TBM: tuberculous meningitis, TST: tuberculin skin test.
§In children aged <5 years, moderate malnutrition was defined as weight-for-age or height-for-age Z-scores ≥-3 and <-2 standard deviations (SD), and severe malnutrition as weight-for-age or height-for-age Z-scores <-3 SD. In children aged 5-14 years, moderate malnutrition was defined as height-for-age or BMI-for-age Z-scores ≥-3 and <-2 SD, and severe malnutrition as height-for-age or BMI-for-age Z-scores <-3 SD (*5*).
¥Diagnostic score was assessed using a uniform case definition criteria for TBM, and was categorized as definite TBM (microbiologically proven from CSF examination), probable TBM (diagnostic score of ≥10 points when cerebral imaging is not available or ≥12 points when cerebral imaging is available), and possible TBM (diagnostic score of 6-9 points when cerebral imaging is not available or 6-11 points when cerebral imaging is available) (*2*).
¶Severity of TBM was classified according to the modified British Medical Research Council grading system as stage I (GCS of 15 with no focal neurologic signs), stage II (GCS of 11-14 or 15 with focal neurologic signs), or stage III (GCS ≤10) (*7*).
§§Analysis was only performed in patients with hydrocephalus
[a]Variables eligible for inclusion in multivariate analysis.
[b,c,d]Due to the likelihood of collinearity (e.g. TBM stage *vs.* GCS score and hydrocephalus *vs.* signs of raised intracranial pressure), only one of each of these variables was included during the development of the final multivariate model.
[e]Even though HIV coinfection was found to be significantly associated with in-hospital death in univariate analysis, we did not include this variable in multivariate analysis due to the selective HIV testing and a very low number of patients with HIV positive (n=4), which might limit the statistical power of the analysis.

**Appendix Table 5.** Univariate logistic regression model for predictors of post-discharge death, tracked until the end of tuberculous meningitis treatment in children treated for tuberculous meningitis at Hasan Sadikin Hospital, Bandung, Indonesia, 2011–2020

| Patient characteristics | Dead (n=18) | Alive (n=91) | cOR (95% CI) | p-value |
|---|---|---|---|---|
| Year of diagnosis (median (IQR)) | 2017 (2015-2018) | 2018 (2016-2019) | 0.96 (0.76-1.20) | 0.703 |
| Year of diagnosis | | | | |
| 2011-2015 | 4 (22.2) | 14 (15.4) | 1.57 (0.45-5.48) | 0.478 |
| 2016-2020 | 14 (77.8) | 77 (84.6) | 1.00 | |
| Age, years (median (IQR)) | 4.0 (2.0-12.2) | 7.0 (1.2-11.0) | 0.98 (0.89-1.09) | 0.752 |
| Age[a] | | | | |
| <2 years | 3 (16.7 ) | 26 (28.6) | 0.65 (0.15-2.86) | 0.573 |
| 2-4 years | 6 (33.3) | 9 (9.9) | 3.78 (0.98-14.56) | 0.054 |
| 5-9 years | 3 (16.7) | 22 (24.2) | 0.77 (0.17-3.41) | 0.734 |
| 10-14 years | 6 (33.3) | 34 (37.4) | 1.00 | |
| Sex[a] | | | | |
| Male | 10 (55.6) | 39 (42.9) | 1.67 (0.60-4.61) | 0.325 |
| Female | 8 (44.4) | 52 (57.1) | 1.00 | |

| Patient characteristics | Dead (n=18) | Alive (n=91) | cOR (95% CI) | p-value |
|---|---|---|---|---|
| Parent's last education | | | | |
|   Junior high school or lower | 9 (50.0) | 40 (44.0) | 1.43 (0.51-4.05) | 0.496 |
|   Senior high school or higher | 8 (44.4) | 51 (56.0) | 1.00 | |
| Parent's monthly income | | | | |
|   USD ≤140,00 | 12 (66.7) | 52 (57.1) | 1.96 (0.58-6.59) | 0.276 |
|   USD >140,00 | 4 (22.2) | 34 (37.4) | 1.00 | |
| Area of living | | | | |
|   Urban | 10 (55.6) | 40 (44.0) | 1.00 | |
|   Rural | 6 (33.3) | 49 (53.8) | 0.49 (0.16-1.46) | 0.201 |
| Weight-for-age Z-score | | | | |
|   ≥-2 (normal) | 6 (33.3) | 34 (37.4) | 1.00 | |
|   <-2 (underweight) | 6 (33.3) | 37 (40.7) | 0.92 (0.27-3.12) | 0.892 |
| Height-for-age Z-score | | | | |
|   ≥-2 (normal) | 11 (61.1) | 53 (58.2) | 1.00 | |
|   <-2 (stunted) | 7 (38.9) | 38 (41.8) | 0.89 (0.31-2.50) | 0.821 |
| Weight-for-height Z-score | | | | |
|   ≥-2 (normal) | 7 (38.9) | 47 (51.6) | 1.00 | |
|   <-2 (wasted) | 11 (61.1) | 44 (48.4) | 1.67 (0.60-4.72) | 0.326 |
| BMI-for-age Z-score | | | | |
|   ≥-2 (normal) | 7 (38.9) | 47 (51.6) | 1.00 | |
|   <-2 (low BMI) | 11 (61.1) | 44 (48.4) | 1.67 (0.60-4.72) | 0.326 |
| Nutritional status[§] | | | | |
|   Normal | 6 (33.3) | 30 (33.0) | 1.00 | |
|   Moderate malnutrition | 7 (38.9) | 29 (31.9) | 1.21 (0.36-4.02) | 0.760 |
|   Severe malnutrition | 5 (27.8) | 32 (35.2) | 0.78 (0.22-2.83) | 0.707 |
| Known BCG vaccination[a] | | | | |
|   No | 7 (38.9) | 15 (16.5) | 3.22 (1.08-9.66) | 0.037 |
|   Yes | 11 (61.1) | 76 (83.5) | 1.00 | |
| Known TB contact history | | | | |
|   No | 13 (72.2) | 68 (74.7) | 1.00 | |
|   Yes | 5 (27.8) | 23 (25.3) | 1.14 (0.37-3.54) | 0.824 |
| *TBM category and stage* | | | | |
|   TBM category[¥] | | | | |
|     Definite TBM | 5 (27.8) | 19 (20.9) | 1.00 | |
|     Probable TBM | 11 (61.1) | 54 (59.3) | 0.77 (0.24-2.52) | 0.670 |
|     Possible TBM | 2 (11.1) | 18 (19.8) | 0.42 (0.07-2.46) | 0.338 |
|   TBM stage[¶,a,b] | | | | |
|     Stage I and II | 7 (38.9) | 67 (73.6) | 1.00 | |
|     Stage III | 11 (61.1) | 24 (26.4) | 4.39 (1.53-12.6) | 0.006 |
|   GCS (median (IQR)) [a,b] | 11 (10-12) | 12 (11-14) | 0.78 (0.64-0.96) | 0.017 |
| *Presenting symptoms* | | | | |
|   Fever | | | | |
|     No | 2 (11.1) | 7 (7.7) | 1.00 | |
|     Yes | 16 (88.9) | 84 (92.3) | 0.67 (0.13-3.51) | 0.632 |
|   Severe headache | | | | |
|     No | 13 (72.2) | 59 (64.8) | 1.00 | |
|     Yes | 4 (22.2) | 30 (33.0) | 0.60 (0.18-2.02) | 0.413 |
|   Muscle weakness | | | | |
|     No | 11 (61.1) | 65 (71.4) | 1.00 | |
|     Yes | 6 (33.3) | 25 (27.5) | 1.42 (0.47-4.24) | 0.532 |
|   Altered consciousness[a] | | | | |
|     No | 1 (5.6) | 25 (27.5) | 1.00 | |
|     Yes | 17 (94.4) | 66 (72.5) | 6.44 (0.81-50.96) | 0.078 |
|   Seizures | | | | |
|     No | 7 (38.9) | 40 (44.0) | 1.00 | |
|     Yes | 11 (61.1) | 51 (56.0) | 1.23 (0.44-3.47) | 0.692 |
|   Shortness of breath | | | | |
|     No | 15 (83.3) | 79 (86.8) | 1.00 | |
|     Yes | 2 (11.1) | 12 (13.2) | 0.88 (0.18-4.33) | 0.873 |
|   Persistent cough | | | | |
|     No | 13 (72.2) | 54 (59.3) | 1.00 | |
|     Yes | 5 (27.8) | 37 (40.7) | 0.56 (0.18-1.71) | 0.309 |
|   Poor weight gain / weight loss | | | | |
|     No | 7 (38.9) | 49 (53.8) | 1.00 | |
|     Yes | 10 (55.6) | 41 (45.1) | 1.71 (0.60-4.88) | 0.319 |
|   Duration of symptoms | | | | |
|     0-7 days | 7 (38.9) | 30 (33.0) | 1.00 | |
|     8-14 days | 8 (44.4) | 50 (54.9) | 0.69 (0.23-2.08) | 0.506 |
|     >14 days | 3 (16.7) | 7 (7.7) | 1.84 (0.38-8.94) | 0.452 |

| Patient characteristics | Dead (n=18) | Alive (n=91) | cOR (95% CI) | p-value |
|---|---|---|---|---|
| *Examination findings at baseline* | | | | |
| Body temperature | | | | |
| <38 °C | 12 (66.7) | 76 (83.5) | 1.00 | |
| ≥38 °C | 6 (33.3) | 15 (16.5) | 2.53 (0.82-7.81) | 0.106 |
| Respiration rate | | | | |
| <25/min | 6 (33.3) | 36 (39.6) | 1.36 (0.47-3.95) | 0.574 |
| ≥25/min | 12 (66.7) | 53 (58.2) | 1.00 | |
| Involuntary movement | | | | |
| No | 16 (88.9) | 80 (87.9) | 1.00 | |
| Yes | 1 (5.6) | 8 (8.8) | 0.62 (0.07-5.35) | 0.668 |
| Cranial nerve palsies | | | | |
| No | 16 (88.9) | 73 (80.2) | 1.00 | |
| Yes | 1 (5.6) | 16 (17.6) | 0.28 (0.03-2.31) | 0.240 |
| Any type of motor deficit | | | | |
| No | 5 (27.8) | 35 (38.5) | 1.00 | |
| Yes | 11 (61.1) | 47 (51.6) | 1.64 (0.52-5.14) | 0.398 |
| Unequal pupils | | | | |
| No | 16 (88.9) | 88 (96.7) | 1.00 | |
| Yes | 1 (5.6) | 1 (1.1) | 5.50 (0.33-92.51) | 0.237 |
| Signs of upper motor neuron lesion | | | | |
| No | 3 (16.7) | 15 (16.5) | 1.00 | |
| Yes | 13 (72.2) | 68 (74.7) | 0.96 (0.24-3.78) | 0.949 |
| Signs of raised intracranial pressure[a,c] | | | | |
| No | 12 (66.7) | 83 (91.2) | 1.00 | |
| Yes | 6 (33.3) | 8 (8.8) | 5.19 (1.53-17.56) | 0.008 |
| *CSF findings* | | | | |
| Leucocyte ≥10 cells/μL | | | | |
| No | 3 (16.7) | 21 (23.1) | 1.00 | |
| Yes | 15 (83.3) | 67 (73.6) | 1.57 (0.41-5.94) | 0.509 |
| Leucocyte ≥100 cells/μL | | | | |
| No | 9 (50.0) | 61 (67.0) | 1.00 | |
| Yes | 9 (50.0) | 27 (29.7) | 2.26 (0.81-6.32) | 0.121 |
| Lymphocytic predominance >50% | | | | |
| No | 3 (16.7) | 18 (19.8) | 1.00 | |
| Yes | 15 (83.3) | 69 (75.8) | 1.30 (0.34-5.00) | 0.698 |
| Protein >100 mg/dL | | | | |
| No | 7 (38.9) | 39 (42.9) | 1.00 | |
| Yes | 11 (61.1) | 49 (53.8) | 1.25 (0.44-3.52) | 0.672 |
| Glucose <40 mg/dL | | | | |
| No | 10 (55.6) | 54 (59.3) | 1.00 | |
| Yes | 7 (38.9) | 29 (31.9) | 1.30 (0.45-3.78) | 0.626 |
| CSF/blood glucose ratio <50% | | | | |
| No | 7 (38.9) | 33 (36.3) | 1.00 | |
| Yes | 7 (38.9) | 35 (38.5) | 0.94 (0.30-2.98) | 0.920 |
| *Radiological findings* | | | | |
| Chest radiography | | | | |
| Normal | 5 (27.8) | 38 (41.8) | 1.00 | |
| Miliary TB | 1 (5.6) | 6 (6.6) | 1.27 (0.12-12.80) | 0.841 |
| Other signs of TB | 12 (66.7) | 47 (51.6) | 1.94 (0.63-5.99) | 0.249 |
| Hydrocephalus[a,c] | | | | |
| No | 3 (16.7) | 66 (72.5) | 1.00 | |
| Yes | 13 (72.2) | 23 (25.3) | 12.43 (3.25-47.59) | <0.001 |
| Neurosurgery in hydrocephalus patients[§§] | | | | |
| No | 11 (84.6) | 10 (43.5) | 7.15 (1.28-39.83) | 0.025 |
| Yes | 2 (15.4) | 13 (56.5) | 1.00 | |
| Basal meningeal enhancement | | | | |
| No | 6 (33.3) | 42 (46.2) | 1.00 | |
| Yes | 10 (55.6) | 47 (51.6) | 1.49 (0.50-4.45) | 0.476 |
| Cerebral infarct | | | | |
| No | 14 (77.8) | 84 (92.3) | 1.00 | |
| Yes | 2 (11.1) | 5 (5.5) | 2.40 (0.42-13.60) | 0.323 |
| Tuberculoma[a] | | | | |
| No | 12 (66.7) | 85 (93.4) | 1.00 | |
| Yes | 4 (22.2) | 4 (4.4) | 7.08 (1.56-32.13) | 0.011 |
| At least 1 sign found on CT scan[a] | | | | |
| No | 1 (5.6) | 29 (31.9) | 1.00 | |
| Yes | 15 (83.3) | 60 (65.9) | 7.25 (0.91-57.58) | 0.061 |
| *Bacteriological findings* | | | | |
| TST positive[a] | | | | |

| Patient characteristics | Dead (n=18) | Alive (n=91) | cOR (95% CI) | p-value |
|---|---|---|---|---|
| No | 10 (55.6) | 76 (83.5) | 1.00 | |
| Yes | 8 (44.4) | 15 (16.5) | 4.05 (1.37-11.96) | 0.011 |
| GeneXpert MTB/RIF testing | | | | |
| Negative | 11 (61.1) | 60 (65.9) | 1.00 | |
| *M.tb* identified from CSF | 5 (27.8) | 19 (20.9) | 1.43 (0.44-4.65) | 0.547 |
| *M.tb* identified from non-CSF | 2 (11.1) | 6 (6.6) | 1.82 (0.32-10.20) | 0.497 |
| AFB smear microscopy | | | | |
| Negative | 15 (83.3) | 74 (81.3) | 1.00 | |
| Positive from CSF | 2 (11.1) | 12 (13.2) | 0.82 (0.17-4.06) | 0.810 |
| Positive from non-CSF | 1 (5.6) | 5 (5.5) | 0.99 (0.11-9.06) | 0.991 |
| *M. tb* cultured from any source | | | | |
| No | 14 (77.8) | 79 (86.8) | 1.00 | |
| Yes | 4 (22.2) | 10 (11.0) | 2.26 (0.62-8.21) | 0.217 |
| *In-hospital complications* | | | | |
| Motor disorders[a] | | | | |
| No | 7 (38.9) | 60 (65.9) | 1.00 | |
| Yes | 11 61.1) | 31 (34.1) | 3.04 (1.07-8.62) | 0.036 |
| Visual impairment | | | | |
| No | 18 (100.0) | 85 (93.4) | 1.00 | |
| Yes | 0 (0.0) | 6 (6.6) | n/a | 0.999 |
| Hearing impairment | | | | |
| No | 18 (100.0) | 87 (95.6) | 1.00 | |
| Yes | 0 (0.0) | 4 (4.4) | n/a | 0.999 |
| Neurodevelopmental delay | | | | |
| No | 16 (88.9) | 80 (87.9) | 1.00 | |
| Yes | 2 (11.1) | 11 (12.1) | 0.91 (0.18-4.50) | 0.907 |
| Epileptic seizures | | | | |
| No | 17 (94.4) | 82 (90.1) | 1.00 | |
| Yes | 1 (5.6) | 9 (9.9) | 0.54 (0.06-4.51) | 0.566 |
| Anti-TB drug-induced hepatotoxicity | | | | |
| No | 14 (77.8) | 76 (83.5) | 1.00 | |
| Yes | 4 (22.2) | 15 (16.5) | 1.45 (0.42-5.01) | 0.559 |
| *Others* | | | | |
| Oral corticosteroid | | | | |
| No | 0 (0.0) | 4 (4.4) | n/a | 0.999 |
| Yes | 17 (94.4) | 85 (93.4) | 1.00 | |
| Physiotherapy | | | | |
| No | 14 (77.8) | 62 (68.1) | 1.73 (0.45-6.58) | 0.421 |
| Yes | 3 (16.7) | 23 (25.3) | 1.00 | |

cOR: crude odds ratio, AFB: acid-fast bacilli, BCG: Bacillus Calmette-Guerin, CSF: cerebrospinal fluid, CI: confidence interval, GCS: Glasgow Coma Scale, IQR: interquartile rage, TB: tuberculosis, TBM: tuberculous meningitis, TST: tuberculin skin test.
[§]In children aged <5 years, moderate malnutrition was defined as weight-for-age or height-for-age Z-scores ≥-3 and <-2 standard deviations (SD), and severe malnutrition as weight-for-age or height-for-age Z-scores <-3 SD. In children aged 5-14 years, moderate malnutrition was defined as height-for-age or BMI-for-age Z-scores ≥-3 and <-2 SD, and severe malnutrition as height-for-age or BMI-for-age Z-scores <-3 SD (*5*).
[¥]Diagnostic score was assessed using a uniform case definition criteria for TBM, and was categorized as definite TBM (microbiologically proven from CSF examination), probable TBM (diagnostic score of ≥10 points when cerebral imaging is not available or ≥12 points when cerebral imaging is available), and possible TBM (diagnostic score of 6-9 points when cerebral imaging is not available or 6-11 points when cerebral imaging is available) (*2*).
[¶]Severity of TBM was classified according to the modified British Medical Research Council grading system as stage I (GCS of 15 with no focal neurologic signs), stage II (GCS of 11-14 or 15 with focal neurologic signs), or stage III (GCS ≤10) (*7*).
[§§]Analysis was only performed in patients with hydrocephalus
[a]Variables eligible for inclusion in multivariate analysis.
[b,c]Due to the likelihood of collinearity (TBM stage *vs.* GCS score and hydrocephalus *vs.* signs of raised intracranial pressure), only one of each of these variables was included during the development of the final multivariate model.


**Appendix Table 6.** Univariate logistic regression model for predictors of severe neurologic sequelae at tuberculous meningitis treatment completion in children treated for tuberculous meningitis at Hasan Sadikin Hospital, Bandung, Indonesia, 2011–2020

| Patient characteristics | Severe neurologic sequelae | | cOR (95% CI) | p-value |
|---|---|---|---|---|
| | Yes (n=33) | No (n=58) | | |
| Year of diagnosis (median (IQR)) | 2018 (2016-2018) | 2018 (2016-2019) | 1.05 (0.86-1.28) | 0.628 |
| Year of diagnosis | | | | |
| 2011-2015 | 3 (9.1) | 11 (19.0) | 0.43 (0.11-1.66) | 0.219 |
| 2016-2020 | 30 (90.9) | 47 (81.0) | 1.00 | |
| Age, years (median (IQR)) | | | 0.93 (0.85-1.02) | 0.138 |
| Age[a] | | | | |
| <2 years | 13 (39.4) | 13 (22.4) | 2.78 (0.94-8.20) | 0.064 |
| 2-4 years | 2 (6.1) | 7 (12.1) | 0.79 (0.14-4.55) | 0.795 |
| 5-9 years | 9 (27.3) | 13 (22.4) | 1.92 (0.61-6.02) | 0.261 |
| 10-14 years | 9 (27.3) | 25 (43.1) | 1.00 | |

| Patient characteristics | Severe neurologic sequelae | | cOR (95% CI) | p-value |
|---|---|---|---|---|
| | Yes (n=33) | No (n=58) | | |
| Sex[a] | | | | |
| Male | 12 (36.4) | 27 (46.6) | 0.66 (0.27-1.58) | 0.346 |
| Female | 21 (63.6) | 31 (53.4) | 1.00 | |
| Parent's last education | | | | |
| Junior high school or lower | 17 (51.5) | 23 (39.7) | 1.62 (0.68-3.82) | 0.275 |
| Senior high school or higher | 16 (48.5) | 35 (60.3) | 1.00 | |
| Parent's monthly income | | | | |
| USD ≤140,00 | 17 (51.5) | 35 (60.3) | 0.69 (0.28-1.70) | 0.424 |
| USD >140,00 | 14 (42.4) | 20 (34.5) | 1.00 | |
| Area of living | | | | |
| Urban | 12 (36.4) | 28 (48.3) | 1.00 | |
| Rural | 20 (60.6) | 29 (50.0) | 1.61 (0.66-3.90) | 0.292 |
| Weight-for-age Z-score | | | | |
| ≥-2 (normal) | 13 (39.4) | 21 (36.2) | 1.00 | |
| <-2 (underweight) | 16 (48.5) | 21 (36.2) | 1.23 (0.48-3.18) | 0.668 |
| Height-for-age Z-score | | | | |
| ≥-2 (normal) | 19 (57.6) | 34 (58.6) | 1.00 | |
| <-2 (stunted) | 14 (42.4) | 24 (41.4) | 1.04 (0.44-2.48) | 0.923 |
| Weight-for-height Z-score | | | | |
| ≥-2 (normal) | 14 (42.4) | 33 (56.9) | 1.00 | |
| <-2 (wasted) | 19 (57.6) | 25 (43.1) | 1.79 (0.75-4.25) | 0.186 |
| BMI-for-age Z-score | | | | |
| ≥-2 (normal) | 14 (42.4) | 33 (56.9) | 1.00 | |
| <-2 (low BMI) | 19 (57.6) | 25 (43.1) | 1.79 (0.75-4.25) | 0.186 |
| Nutritional status[§] | | | | |
| Normal | 9 (27.3) | 21 (36.2) | 1.00 | |
| Moderate malnutrition | 12 (36.4) | 17 (29.3) | 1.65 (0.56-4.83) | 0.363 |
| Severe malnutrition | 12 (36.4) | 20 (34.5) | 1.40 (0.48-4.04) | 0.534 |
| Known BCG vaccination | | | | |
| No | 3 (9.1) | 12 (20.7) | 0.38 (0.10-1.47) | 0.163 |
| Yes | 30 (90.9) | 46 (79.3) | 1.00 | |
| Known TB contact history | | | | |
| No | 25 (75.8) | 43 (74.1) | 1.00 | |
| Yes | 8 (24.2) | 15 (25.9) | 0.92 (0.34-2.47) | 0.864 |
| *TBM category and stage* | | | | |
| TBM category[¥] | | | | |
| Definite TBM | 6 (18.2) | 13 (22.4) | 1.00 | |
| Probable TBM | 22 (66.7) | 32 (55.2) | 1.49 (0.49-4.52) | 0.481 |
| Possible TBM | 5 (15.2) | 13 (22.4) | 0.83 (0.20-3.43) | 0.800 |
| TBM stage[¶,a] | | | | |
| Stage I | 5 (15.2) | 17 (29.3) | 1.00 | |
| Stage II | 14 (42.4) | 31 (53.4) | 1.53 (0.47-5.00) | 0.476 |
| Stage III | 14 (42.4) | 10 (17.2) | 4.76 (1.32-17.22) | 0.017 |
| GCS (median (IQR)) | | | 0.91 (0.76-1.09) | 0.316 |
| *Presenting symptoms* | | | | |
| Fever | | | | |
| No | 2 (6.1) | 5 (8.6) | 1.00 | |
| Yes | 31 (93.9) | 53 (91.4) | 1.46 (0.27-7.99) | 0.661 |
| Severe headache | | | | |
| No | 23 (69.7) | 36 (62.1) | 1.00 | |
| Yes | 9 (27.3) | 21 (36.2) | 0.67 (0.26-1.72) | 0.405 |
| Muscle weakness | | | | |
| No | 23 (69.7) | 42 (72.4) | 1.00 | |
| Yes | 9 (27.3) | 16 (27.6) | 1.03 (0.39-2.69) | 0.956 |
| Altered consciousness | | | | |
| No | 9 (27.3) | 16 (27.6) | 1.00 | |
| Yes | 24 (72.7) | 42 (72.4) | 1.02 (0.39-2.65) | 0.974 |
| Seizures | | | | |
| No | 13 (39.4) | 27 (46.6) | 1.00 | |
| Yes | 20 (60.6) | 31 (53.4) | 1.34 (0.56-3.19) | 0.509 |
| Shortness of breath | | | | |
| No | 30 (90.9) | 49 (84.5) | 1.00 | |
| Yes | 3 (9.1) | 9 (15.5) | 0.54 (0.14-2.17) | 0.389 |
| Persistent cough | | | | |
| No | 21 (63.6) | 33 (56.9) | 1.00 | |
| Yes | 12 (36.4) | 25 (43.1) | 0.75 (0.31-1.82) | 0.530 |
| Poor weight gain / weight loss | | | | |
| No | 14 (42.4) | 35 (60.3) | 1.00 | |

| Patient characteristics | Severe neurologic sequelae | | cOR (95% CI) | p-value |
|---|---|---|---|---|
| | Yes (n=33) | No (n=58) | | |
| Yes | 18 (54.5) | 23 (39.7) | 1.96 (0.82-4.69) | 0.132 |
| Duration of symptoms | | | | |
| 0-7 days | 14 (42.4) | 16 (27.6) | 1.00 | |
| 8-14 days | 16 (48.5) | 34 (58.6) | 0.54 (0.21-1.36) | 0.192 |
| >14 days | 3 (9.1) | 4 (6.9) | 0.86 (0.16-4.51) | 0.856 |
| *Examination findings at baseline* | | | | |
| Body temperature | | | | |
| <38 °C | 23 (69.7) | 53 (91.4) | 1.00 | |
| ≥38 °C | 10 (30.3) | 5 (8.6) | 4.61 (1.42-14.99) | 0.011 |
| Respiration rate | | | | |
| <25/min | 12 (36.4) | 24 (41.4) | 1.00 | |
| ≥25/min | 21 (63.6) | 32 (55.2) | 1.31 (0.54-3.18) | 0.547 |
| Involuntary movement | | | | |
| No | 29 (87.9) | 51 (87.9) | 1.00 | |
| Yes | 4 (12.1) | 4 (6.9) | 1.76 (0.41-7.56) | 0.448 |
| Cranial nerve palsies | | | | |
| No | 26 (78.8) | 47 (81.0) | 1.00 | |
| Yes | 7 (21.2) | 9 (15.5) | 1.41 (0.47-4.21) | 0.543 |
| Any type of motor deficit[a] | | | | |
| No | 8 (24.2) | 27 (46.6) | 1.00 | |
| Yes | 24 (72.7) | 23 (39.7) | 3.52 (1.33-9.33) | 0.011 |
| Unequal pupils | | | | |
| No | 32 (97.0) | 56 (96.6) | 1.00 | |
| Yes | 1 (3.0) | 0 (0.0) | n/a | 1.000 |
| Signs of upper motor neuron lesions | | | | |
| No | 5 (15.2) | 10 (17.2) | 1.00 | |
| Yes | 27 (81.8) | 41 (70.7) | 1.32 (0.40-4.28) | 0.647 |
| Signs of raised intracranial pressure | | | | |
| No | 31 (93.9) | 52 (89.7) | 1.00 | |
| Yes | 2 (6.1) | 6 (10.3) | 0.56 (0.11-2.94) | 0.493 |
| *CSF findings* | | | | |
| Leucocyte ≥10 cells/µL | | | | |
| No | 9 (27.3) | 12 (20.7) | 1.00 | |
| Yes | 23 (69.7) | 44 (75.9) | 0.70 (0.26-1.90 | 0.479 |
| Leucocyte ≥100 cells/µL | | | | |
| No | 24 (72.7) | 37 (63.8) | 1.00 | |
| Yes | 8 (24.2) | 19 (32.8) | 0.65 (0.24-1.72) | 0.384 |
| Lymphocytic predominance >50% | | | | |
| No | 9 (27.3) | 9 (15.5) | 1.00 | |
| Yes | 23 (69.7) | 46 (79.3) | 0.50 (0.17-1.43) | 0.196 |
| Protein >100 mg/dL | | | | |
| No | 11 (33.3) | 28 (48.3) | 1.00 | |
| Yes | 21 (63.6) | 28 (48.3) | 1.91 (0.78-4.69) | 0.158 |
| Glucose <40 mg/dL | | | | |
| No | 20 (60.6) | 34 (58.6) | 1.00 | |
| Yes | 12 (36.4) | 17 (29.3) | 1.20 (0.48-3.02) | 0.699 |
| CSF/blood glucose ratio <50% | | | | |
| No | 13 (39.4) | 20 (34.5) | 1.00 | |
| Yes | 15 (45.5) | 20 (34.5) | 1.15 (0.44-3.04) | 0.772 |
| *Radiological findings* | | | | |
| Chest radiography[a] | | | | |
| Normal | 9 (27.3) | 29 (50.0) | 1.00 | |
| Miliary TB | 3 (9.1) | 3 (5.2) | 3.22 (0.55-18.85) | 0.194 |
| Other signs of TB | 21 (63.6) | 26 (44.8) | 2.60 (1.01-6.68) | 0.047 |
| Hydrocephalus[a] | | | | |
| No | 22 (66.7) | 44 (75.9) | 1.00 | |
| Yes | 11 (33.3) | 12 (20.7) | 1.83 (0.70-4.81) | 0.218 |
| Neurosurgery in hydrocephalus patients[§§] | | | | |
| No | 4 (36.4) | 6 (50.0) | 0.57 (0.11-3.04) | 0.511 |
| Yes | 7 (63.6) | 6 (50.0) | 1.00 | |
| Basal meningeal enhancement | | | | |
| No | 14 (42.4) | 28 (48.3) | 1.00 | |
| Yes | 19 (57.6) | 28 (48.3) | 1.36 (0.57-3.23) | 0.490 |
| Cerebral infarct | | | | |
| No | 30 (90.9) | 54 (93.1) | 1.00 | |
| Yes | 3 (9.1) | 2 (3.4) | 2.70 (0.43-17.07) | 0.291 |
| Tuberculoma | | | | |
| No | 31 (93.9) | 54 (93.1) | 1.00 | |

| Patient characteristics | Severe neurologic sequelae | | cOR (95% CI) | p-value |
|---|---|---|---|---|
| | Yes (n=33) | No (n=58) | | |
| Yes | 2 (6.1) | 2 (3.4) | 1.74 (0.23-12.99) | 0.588 |
| At least 1 sign found on CT scan[a] | | | | |
| No | 7 (21.2) | 22 (37.9) | 1.00 | |
| Yes | 26 (78.8) | 34 (58.6) | 2.40 (0.89-6.48) | 0.083 |
| *Bacteriological findings* | | | | |
| TST positive | | | | |
| No | 26 (78.8) | 50 (86.2) | 1.00 | |
| Yes | 7 (21.2) | 8 (13.8) | 1.68 (0.55-5.15) | 0.362 |
| GeneXpert MTB/RIF testing | | | | |
| Negative | 23 (69.7) | 37 (63.8) | 1.00 | |
| *M.tb* identified from CSF | 6 (18.2) | 13 (22.4) | 0.74 (0.25-2.23) | 0.595 |
| *M.tb* identified from non-CSF | 4 (12.1) | 2 (3.4) | 3.22 (0.54-18.99) | 0.197 |
| AFB smear microscopy[a] | | | | |
| Negative | 23 (69.7) | 51 (87.9) | 1.00 | |
| Positive from non-CSF | 8 (24.2) | 4 (6.9) | 4.43 (1.21-16.23) | 0.024 |
| *M. tb* cultured from any source | | | | |
| No | 28 (84.8) | 51 (87.9) | 1.00 | |
| Yes | 5 (15.2) | 5 (8.6) | 1.82 (0.48-6.84) | 0.374 |
| *Others* | | | | |
| Anti-TB drug-induced hepatotoxicity | | | | |
| No | 29 (87.9) | 47 (81.0) | 1.00 | |
| Yes | 4 (12.1) | 11 (19.0) | 0.59 (0.17-2.02) | 0.401 |
| Oral corticosteroid | | | | |
| No | 0 (0.0) | 4 (6.9) | n/a | 0.999 |
| Yes | 33 (100.0) | 52 (89.7) | 1.00 | |
| Physiotherapy | | | | |
| No | 21 (63.6) | 41 (70.7) | 0.56 (0.21-1.48) | 0.241 |
| Yes | 11 (33.3) | 12 (20.7) | 1.00 | |

cOR: crude odds ratio, AFB: acid-fast bacilli, BCG: Bacillus Calmette-Guerin, CSF: cerebrospinal fluid, CI: confidence interval, GCS: Glasgow Coma Scale, IQR: interquartile rage, TB: tuberculosis, TBM: tuberculous meningitis, TST: tuberculin skin test.
§In children aged <5 years, moderate malnutrition was defined as weight-for-age or height-for-age Z-scores ≥-3 and <-2 standard deviations (SD), and severe malnutrition as weight-for-age or height-for-age Z-scores <-3 SD. In children aged 5-14 years, moderate malnutrition was defined as height-for-age or BMI-for-age Z-scores ≥-3 and <-2 SD, and severe malnutrition as height-for-age or BMI-for-age Z-scores <-3 SD (5).
¥Diagnostic score was categorized as definite TBM (microbiologically proven from CSF examination), probable TBM (diagnostic score of ≥10 points when cerebral imaging is not available or ≥12 points when cerebral imaging is available), and possible TBM (diagnostic score of 6-9 points when cerebral imaging is not available or 6-11 points when cerebral imaging is available) (2).
¶Severity of TBM was classified as stage I (GCS of 15 with no focal neurologic signs), stage II (GCS of 11-14 or 15 with focal neurologic signs), or stage III (GCS ≤10) (7).
§§Analysis was only performed in patients with hydrocephalus
[a]Variables eligible for inclusion in multivariate analysis.

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