223

# Xpert MTB/RIF Assay for Diagnosis of Tuberculous Meningitis (TBM) in Maharaj Nakorn Chiang Mai Hospital

Poramed Winichakoon, M.D.[1] , Parichat Salee, M.D.[1] , Kanokwan Watcharasaksilp, M.D.[1] , Romanee Chaiwarith, M.D.[1] , Nontakarn Nuntachit, M.D.[1] , Quanhathai Kaewpoowat, M.D.[2] , Kanlaya Wongworapat, M.Sc.[2] , Chansom Pantip, M.Sc.[2] , Sunisa Butphet, M.Sc.[2] , Vilai Boasoung, M.Sc. , Banyong Khantawa, M.Sc. , Phadungkiat Khamnoi, M.Sc. , Khuanchai Supparatpinyo, M.D.[1,2], and Thira Sirisanthana, M.D.[2]

[1]Maharaj Nakorn Chiang Mai Hospital, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, [2]Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand

Email: poramed.win@gmail.com
Mailing address: 110 Intavaroros, Sribhoom, Muang, Chiang Mai, Thailand.
Tel +66-5394-6457
Fax +66-5389-4231

## BACKGROUND

- Early diagnosis and treatment of tuberculous meningitis (TBM) are crucial steps to reduce morbidity and mortality.
- The accuracy of using Xpert MTB/RIF assay for the diagnosis of TBM is still questionable.
- This study aimed to find out the diagnostic performance of Xpert MTB/RIF assay for the diagnosis of tuberculous meningitis.

## METHODS

A prospective cohort study was conducted at Maharaj Nakorn Chiang Mai Hospital, Thailand. Patients who were ≥15 years old and had subacute lymphocytic meningitis were included.

- Inclusion criteria: A plus 2 of 3 from B
  - A. Duration of symptoms ≥ 5 days
  - B. Presence of CSF findings of TBM:
    - (i) Lymphocytic-predominant pleocytosis
    - (ii) Elevated protein levels
    - (iii) CSF: plasma glucose ratio <0.5
- Exclusion criteria: any of the following
  - A. Any contraindications for lumbar puncture
  - B. Denial of treatment or procedure
  - C. CSF positive for Cryptococcal antigen titer

## METHODS

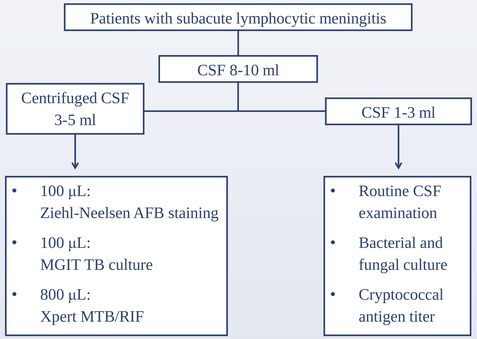


Figure 1: Flow chart for CSF specimen processing

| Tuberculous meningitis classification | |
|---|---|
| Clinical criteria | One or more of the compatible symptoms and signs |
| Definite TBM | A) Clinical criteria plus one or more of the following: AFB seen in CSF; *M. tuberculosis* cultured from CSF<br>B) Acid-fast bacilli seen from pathological change consistent with TBM in the brain or spinal cord. |
| Probable TBM | Clinical criteria plus total diagnostic score of 10 or more (when neuroimaging not available) or 12 or more points (when neuroimaging available)<br>plus exclusion of alternative diagnoses. |
| Possible TBM | Clinical criteria plus a total diagnostic score of 6–9 (when neuroimaging not available) or 6–11 points (when neuroimaging available)<br>plus exclusion of alternative diagnoses.<br>Possible TBM cannot be diagnosed or excluded without doing a lumbar puncture or neuroimaging. |
| Not TBM | Not meeting the criteria, plus alternative diagnosis established without other clues of dual disease. |

Table 1: Eligible study population were classified as having definite, probable, possible, or not TBM.
(Adapted from a uniform case definition for clinical research by *Marais S et al* in Lancet Infectious Diseases, 2010)

## RESULTS

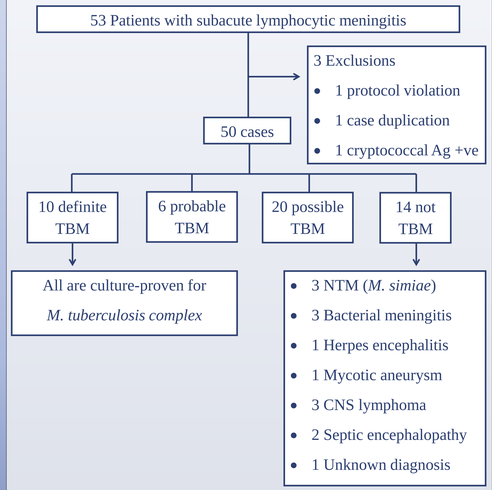


Figure 2: Diagnostic schema of study population

| | Parameter | Frequency, % |
|---|---|---|
| **Gender** | Male | 25 (50%) |
| **Co-morbidities** | Immunosuppressive drugs | 11 (22%) |
| | HIV infection | 11 (22%) |
| **Clinical characteristics** | Fever | 31 (62%) |
| | Alteration of consciousness | 28 (56%) |
| | Headache | 20 (40%) |
| | Weakness | 13 (26%) |
| | Neck stiffness | 10 (20%) |
| **Neuroimaging findings** | Communicating hydrocephalus | 20 (40%) |
| | Leptomeningeal enhancement | 18 (36%) |
| | Brain infarction | 8 (16%) |
| | Tuberculoma | 3 (6%) |

Table 2: Demographic data of study population

## RESULTS

| Diagnostic value (95% CI) | Test | | |
|---|---|---|---|
| | Xpert MTB/RIF | AFB staining | TBM score ≥ 6 |
| **Sensitivity** | 80% (44.39-97.48) | 0% (0-30.85) | 100% (69.15-100) |
| **Specificity** | 97.5% (86.84-99.94) | 100% (91.19-100) | 25% (12.69-41.20) |
| **PPV** | 88.89% (51.75-99.72) | - | 25% (12.69-41.20) |
| **NPV** | 95.12% (83.47-99.40) | 80% (66.28-89.97) | 100% (69.15- 100) |

Table 3: Diagnostic performances of Xpert MTB/RIF assay, AFB staining, and TBM score compared with culture-proven TBM, Xpert MTB/RIF assay had significantly higher sensitivity ($p$ <0.001) than AFB staining, and higher specificity ($p$ <0.001) than TBM score. There was a good concordance between Xpert MTB/RIF assay and MGIT TB culture with 94% agreement (p < 0.001).

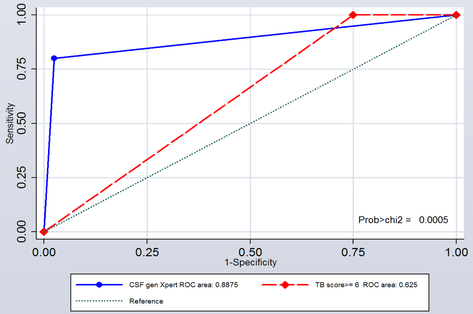


Figure 3: ROC Curve for sensitivity and 1-specificity of Xpert MTB/RIF assay and the TBM score compared with the MGIT culture.

## RESULTS

| Testing | Diagnostic values | |
|---|---|---|
| | Sensitivity | Specificity |
| **TBM score ≥ 6** | 100% | 25% |
| **Xpert MTB/RIF** | 80% | 97.5% |
| **Sequential testing** | Net Sensitivity = 80% | Net Specificity = 98.13% |

Table 4: Using a TBM score at cut-point of 6, and then Xpert MTB/RIF assay as the sequential testing, there was an improvement in specificity.

## CONCLUSIONS

- Centrifuged CSF Xpert MTB/RIF assay was a rapid test to detect *M. tuberculosis complex* from CSF with high sensitivity and specificity.
- The TBM scoring system could be used as a screening test before using a more specific diagnosis test for TBM patients .
- This sequential testing may be useful as a diagnostic algorithm for rapid diagnosis of TBM.

## ACKNOWNLEDGEMENTS

- Research Administration Committee, Faculty of Medicine, Chiang Mai University
- Research Institute for Health Sciences, Chiang Mai University
- Infectious Disease Association of Thailand