

## VALIDASI UJI *POLYMERASE CHAIN REACTION* MULTIPLEKS DAN XPERT MTB/RIF UNTUK DETEKSI PATOGEN PENYEBAB INFEKSI SISTEM SARAF PUSAT

Bardatin Lutfi Aifa<sup>\*a</sup>, Ismail Setyopranoto<sup>\*\*</sup>, Sekar Satiti<sup>\*\*</sup>

<sup>\*</sup>Residen Neurologi Fakultas Kedokteran, Kesehatan Masyarakat, dan Keperawatan Universitas Gadjah Mada

<sup>\*\*</sup>Staff Departemen Neurologi Fakultas Kedokteran, Kesehatan Masyarakat, dan Keperawatan Universitas Gadjah Mada/KSM Saraf RSUP Dr. Sardjito Yogyakarta

<sup>a</sup>Korespondensi: [bardatin.aifa@ugm.ac.id](mailto:bardatin.aifa@ugm.ac.id)

### ABSTRAK

**Latar belakang:** Infeksi sistem saraf pusat (SSP) masih merupakan masalah kesehatan penting di Indonesia dengan morbiditas dan mortalitas yang tinggi. Beberapa etiologi utama meliputi *Mycobacterium tuberculosis*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Cryptococcus species*, *herpes simplex virus* tipe-1 (HSV-1), dan tipe-2 (HSV-2). Uji MTB/RIF Xpert dapat mendeteksi *M. tuberculosis* pada cairan serebrospinal (CSS) dengan cepat, tetapi memiliki sensitivitas yang rendah. *Polymerase chain reaction* (PCR) multipleks *Biofire® FilmArray® Meningitis/Encephalitis* (ME) panel dapat mendeteksi 14 patogen penyebab tersering infeksi SSP, tetapi belum didapatkan penelitian mengenai nilai diagnostiknya di Indonesia.

**Tujuan:** Melakukan uji diagnostik PCR multipleks *Biofire® FilmArray® ME panel* dalam mendeteksi *S. pneumoniae*; *N. meningitidis*; HSV-1; HSV-2; dan *C. neoformans*; serta melakukan uji diagnostik Xpert MTB/RIF dalam mendeteksi *M. tuberculosis*.

**Metode:** Penelitian ini menggunakan sampel CSS dari pasien dewasa dengan klinis infeksi SSP yang dirawat di RSUP Dr. Sardjito pada September 2022 – Agustus 2023. Sensitivitas / *positive percentage of agreement* (PPA) dan spesifisitas / *negative percentage of agreement* (NPA) dari PCR multipleks dan Xpert MTB/RIF dinilai dengan uji pembandingan PCR spesifik patogen dan *Cryptococcus antigen lateral flow assay*.

**Hasil:** Sebanyak 50 pasien (median usia 35 tahun, 60% laki-laki) disertakan dalam analisis penelitian. Uji Xpert MTB/RIF memiliki PPA 100% dan NPA 97,5% dalam mendeteksi *M. tuberculosis*, sedangkan uji PCR multipleks memiliki PPA 100% dan NPA 100% dalam mendeteksi *C. neoformans*. Tidak didapatkan sampel yang terdeteksi positif terhadap *S. pneumoniae*, *N. meningitidis*, HSV-1, dan HSV-2, sehingga PPA/sensitivitas dan NPA/spesifisitas PCR multipleks dalam mendeteksi patogen tersebut tidak dapat dinilai.

**Kesimpulan:** Belum didapatkan bukti kebermanfaatan yang bermakna dari PCR multipleks *Biofire® FilmArray® ME panel* dalam mendeteksi patogen penyebab infeksi SSP di RSUP Dr. Sardjito. Uji Xpert MTB/RIF dapat direkomendasikan sebagai pemeriksaan lini pertama dalam deteksi *M. tuberculosis* pada CSS dan menjadi acuan diagnosis infeksi tuberkulosis SSP.

**Kata kunci:** infeksi sistem saraf pusat, meningitis, ensefalitis, PCR multipleks, Xpert MTB/RIF

## VALIDATION OF MULTIPLEX POLYMERASE CHAIN REACTION AND XPRT MTB/RIF ASSAYS FOR THE DETECTION OF PATHOGENS CAUSING CENTRAL NERVOUS SYSTEM INFECTION

Bardatin Lutfi Aifa<sup>\*a</sup>, Ismail Setyopranoto<sup>\*\*</sup>, Sekar Satiti<sup>\*\*</sup>

<sup>\*</sup>Neurology Resident, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada,  
Yogyakarta, Indonesia

<sup>\*\*</sup>Neurology Department, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada /  
Sardjito General Hospital, Yogyakarta, Indonesia

<sup>a</sup>Corresponding Author: Bardatin Lutfi Aifa, e-mail: [bardatin.aifa@ugm.ac.id](mailto:bardatin.aifa@ugm.ac.id)

### ABSTRACT

**Background:** Central nervous system (CNS) infection remains a major health problem in Indonesia with high morbidity and mortality. Some of the main etiologies include *Mycobacterium tuberculosis*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Cryptococcus species*, *herpes simplex virus* type-1 (HSV-1), and type-2 (HSV-2). The MTB/RIF Xpert assay can detect *M. tuberculosis* in cerebrospinal fluid (CSF) rapidly, however it has low sensitivity. The Biofire® FilmArray® Meningitis/Encephalitis (ME) panel multiplex polymerase chain reaction (PCR) can detect 14 common pathogens causing CNS infections, however its diagnostic value in Indonesia has not been validated.

**Objective:** To perform diagnostic test on the Biofire® FilmArray® ME panel PCR for the detection of *S. pneumoniae*; *N. meningitidis*; HSV-1; HSV-2; and *C. neoformans*; and to perform diagnostic test on the Xpert MTB/RIF assay for *M. tuberculosis* detection.

**Methods:** This study used CSF samples from adult patients with clinical CNS infections admitted to Dr. Sardjito General Hospital in September 2022 – August 2023. The sensitivity / positive percentage of agreement (PPA) and specificity / negative percentage of agreement (NPA) of multiplex PCR and Xpert MTB/RIF assays were assessed using comparative tests of pathogen-specific PCR and *Cryptococcus* antigen lateral flow assay.

**Results:** A total of 50 patients (median age 35 years, 60% male) were included in the study analysis. The Xpert MTB/RIF test had a PPA of 100% and an NPA of 97.5% in detecting *M. tuberculosis*, while the multiplex PCR test had both PPA and NPA of 100% in detecting *C. neoformans*. No samples were detected positive for *S. pneumoniae*, *N. meningitidis*, HSV-1, and HSV-2, thus the PPA/sensitivity and NPA/specificity of the multiplex PCR in detecting these pathogens were undetermined.

**Conclusion:** There is no significant evidence of the Biofire® FilmArray® ME panel multiplex PCR efficacy in detecting pathogens causing CNS infections at Dr. Sardjito General Hospital. The Xpert MTB/RIF test could be recommended as a first-line investigation in detecting *M. tuberculosis* in CSF and as a reference for diagnosing CNS tuberculosis infection.

**Keywords:** central nervous system infections, meningitis, encephalitis, multiplex PCR, Xpert MTB/RIF